

Università degli Studi di Sassari



Alta Formazione

Scuola di Dottorato di Ricerca  
dell'Università degli Studi di Sassari



**Riassunti delle Tesi**

***Thesis Abstracts***

Cerimonia di Consegna delle Pergamene di  
Dottore di Ricerca dell'A.A. 2017/2018

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A cura di Antonello Cannas, Anna Paola Vargiu, Riccardo Zallu, Elisa Campus

Scuola di Dottorato di Ricerca dell'Università degli Studi di Sassari

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# Presentazione

La ricerca, quella libera, non immediatamente orientata o peggio asservita a logiche politiche o di profitto, è l'unica in grado di produrre i risultati scientifici più alti: l'indipendenza dei ricercatori, dell'Università e degli enti di ricerca è un bene da preservare ad ogni costo. L'Università degli Studi di Sassari, da sempre, persegue questo fine. Lo sancisce l'articolo 2 dello statuto e lo confermano i lavori dei nostri futuri dottori di ricerca, che si sono dimostrati all'altezza delle aspettative di un sistema universitario di primissimo livello.

L'Università di Sassari continua ad essere uno spazio di sperimentazione avanzata di linee di ricerca radicate e coltivate all'interno dei corsi di laurea e in questo ha avuto un ruolo determinante la Scuola di Dottorato, che riunisce 10 corsi dottorali, con più di 15 curricula nei diversi settori disciplinari.

La curiosità è il motore della conoscenza senza la quale non si impara né si insegna, è la motivazione che ci spinge a incrementare il sapere, è un bisogno innato che si sviluppa in relazione alle esperienze che possono favorirla o reprimerla. La scuola dottorale, nel tempo, ha stretto relazioni con enti e università straniere, anche attraverso la pratica della cotutela. È per questo che la nostra scuola spinge i nostri studenti a conoscere altre realtà e contesti culturali.

Le brevi presentazioni delle ricerche condotte dai nostri studenti, racchiuse in questo opuscolo, dimostrano la vitalità della ricerca, unico grande motore che permette di aprire nuovi e fecondi orizzonti di indagine.

Quest'anno ricorrono i 500 anni della nascita di Leonardo da Vinci. Pittore, scultore, inventore, ingegnere militare, scenografo, anatomista, pensatore, uomo di scienza. Leonardo è l'archetipo dell'uomo del Rinascimento, di cui incarna l'aspirazione di conoscenza del reale attraverso la ragione e l'esperienza; ma non solo, il suo genio creativo e la sua insaziabile curiosità, rappresentano qualcosa di universale: l'innato desiderio dell'uomo di superare i propri limiti. Forse i tempi che viviamo non sembrano promettere un nuovo Rinascimento; ma a maggior ragione è necessario che i giovani tengano vivi e presenti i valori seguiti da Leonardo: scienza, cultura e libertà.

*IL RETTORE*

*Prof. Massimo Carpinelli*

# Presentation

Free research, when not immediately oriented or, even worse, enslaved to political or profit logics, is the only one able to produce the best scientific results. In fact, the independence of researchers, university, and research institutes is a good to be preserved at any cost.

The University of Sassari has always pursued this goal, as indicated in Article 2 of our Statute and confirmed by the research conducted by our Ph.D. students, who have fulfilled the expectations of a high-quality university system.

The University of Sassari continues to be a place for advanced research topics, explored initially in its Bachelor degrees and further developed in the Ph.D. degree. Therefore, advanced research have had a fundamental role in our Ph.D. School, which currently has 10 Ph.D. programs, with more than 15 curricula in different research areas.

Curiosity is the main driver of knowledge. It is essential for both learning and teaching and generates motivation for increasing knowledge. Curiosity is an innate need dependent on experiences that can favour or discourage its development. Over time our Ph.D. School has made connections with foreign institutes of research and universities in different ways, including the development of thesis in co-tutorship, in order to stimulate our students to live new situations and cultural experiences.

This booklet contains short presentations of the research conducted by our Ph.D. students and shows the vitality of our research environment, which is the only big driver to open new and fertile research horizons.

The year 2019 is the 500<sup>th</sup> year from the birth of Leonardo da Vinci, a painter, sculptor, inventor, military engineer, scenographer, anatomist, intellectual, and man of science. Leonardo was the archetype of the Renaissance man and embodied his aspiration for knowledge of the real world through reason and experience. The creative genius and insatiable curiosity of Leonardo represent something universal: the innate desire of humans to exceed their limits. The times we are living do not seem to announce a new Renaissance and, for this reason, it is even more important that young people keep the values of Leonardo, science, culture and freedom, alive.

The Rector

*Prof. Massimo Carpinelli*

# La Scuola di Dottorato dell'Università degli Studi di Sassari

La Scuola di Dottorato di Ricerca dell'Università degli Studi di Sassari è nata per promuovere, coordinare e migliorare le attività dei dieci Corsi di dottorato dell'Ateneo e dei loro 218 dottorandi, con il fine ultimo di promuovere e perseguire l'eccellenza nel campo formativo e della ricerca.

La Scuola ha come organi il Direttore (Prof. Antonello Cannas) ed il Consiglio della Scuola, costituito dai Coordinatori dei Corsi di dottorato (Proff. Fiammetta Berlinguer, Michele Comenale Pinto, Stefano Enzo, Ignazio Floris, Ludovico Marinò, Massimo Onofri, Vincenzo Pascucci, Andrea Piana, Leonardo Sechi, Raimondo Zucca) e da due rappresentanti dei Dottorandi, uno di area umanistica (dott.ssa Maria Cristina Idini) e uno di area scientifica (dott. Cristiano Depalmas). La Scuola di dottorato è supportata dall'Ufficio Alta Formazione (dott.ssa Anna Paola Vargiu, Responsabile dell'Ufficio; dott. Riccardo Zallu, Referente per i Corsi di Dottorato di ricerca; dott.ssa Elisa Campus, Segretaria della Scuola).

Gli obiettivi della scuola di dottorato sono di: offrire a dottorandi, dottori di ricerca ed docenti un servizio amministrativo centralizzato; organizzare attività didattiche e formative comuni, condivise da tutti i corsi di dottorato, e collaborare alle attività didattiche specifiche di ciascun Corso di dottorato; favorire l'interazione fra settori disciplinari diversi, gli scambi culturali e la creazione di un clima di studio e lavoro aperto, stimolante e creativo; promuovere gli scambi internazionali e l'ingresso di studenti stranieri; promuovere le interazioni e gli scambi col sistema produttivo e l'inserimento dei dottori di ricerca nel mondo del lavoro.

In questo senso come Scuola pensiamo sia importante dare il giusto riconoscimento alle attività di ricerca condotte, con grande dedizione e sacrificio, dai dottori di ricerca del nostro Ateneo. Questo volume è quindi un modo per ringraziare tutti loro per l'impegno ed i risultati conseguiti, ma rappresenta anche una delle diverse azioni che la Scuola di Dottorato intende condurre per divulgare le loro competenze e le loro ricerche nella comunità scientifica e facilitarne il trasferimento negli enti pubblici e nel sistema produttivo.

Il Direttore

*Prof. Antonello Cannas*

# The Ph.D. School of the University of Sassari

The Ph.D. School of the University of Sassari was created to promote, coordinate, and improve the activities of its 10 Ph.D. programs and 218 Ph.D. students, with the final purpose of promoting excellence in education and research.

The School is governed by its Director (Prof. Antonello Cannas), by the School Committee, composed of the Coordinators of the Ph.D. Programs (Professors Fiammetta Berlinguer, Michele Comenale Pinto, Stefano Enzo, Ignazio Floris, Ludovico Marinò, Massimo Onofri, Vincenzo Pascucci, Andrea Piana, Leonardo Sechi and Raimondo Zucca), and by the representatives of the Ph.D. students, one for the humanities area (Maria Cristina Idini) and one for the scientific area (Cristiano Depalmas). The School is supported by the office for Higher Education (Anna Paola Vargiu, Director of the Office; Riccardo Zallu, Referent for the School; and Elisa Campus, Secretariat of the School).

The objectives of the School are to offer a centralized administrative service to Ph.D. students, Ph.D.s. and professors of the School, to organize common teaching and formative activities for all Ph.D. programs and support their own educational activities, to favour the interaction among different disciplinary fields and the creation of an open, stimulating and creative research environment, to promote international exchanges and the internationalisation of the School, to promote exchanges between the university and the productive system during the Ph.D. studies, and to stimulate the employment of Ph.D.s in research institutions and in the private sector.

As a School we believe that it is important to recognize the research activities conducted by the new Ph.D.s. of our University with great effort and dedication. This volume is dedicated to them, as an acknowledgement of their commitment and the results achieved. It also represents one of the many actions that the Ph.D. School of the University of Sassari is performing to spread the skills and the research of our graduate students throughout the scientific and productive community.

The Director

*Prof. Antonello Cannas*

Corso di Dottorato in  
Architettura e Ambiente

—

Ph.D. Program in Architecture and  
Environment

Coordinatore/Coordinator: Prof. Vincenzo Pascucci

Dottori di Ricerca/Ph.D.

Nađa Beretić

Giovanni Campus

Silvia Farris

Omar Sosa Garcia

Roberta Guido

Dottore di Ricerca/Ph.D.: **Nađa Beretić**

Data di Discussione della Tesi/Date of Thesis Defense: **2.3.2018**

Titolo della Tesi/Thesis Title: "**Production of Space: Reproduction of Mining Landscape in Sardinia**"

Tutor/Adviser: **Arnaldo Cecchini**; Co-Tutor/Co-Adviser: **Zoran Đukanović**

### **Abstract**

The research examined mining landscape in Sardinia (Geo-mining, Historical and Environmental Park in Sardinia) as a place for everyday living. Developed within the theoretical framework of 'production of space' and cultural landscape concept, it challenged place to identify and public participation in heritage conservation. Topicspecific theoretical principles and cases of practice have shown the central role of everyday life routine and public participation in making-decision process for long-term heritage sustainability. Comprehensive elaboration of mining landscape in Sardinia confirmed domination of abstract space (bureaucracy and economy - mining industry in the past) that has modelled the landscape ever since. Productive synthesis of theoretical findings and international practices complemented the guidelines for the Sardinian case. Reproduction model illustrated components to the interpretative, evaluative and transformative value of mining landscape in Sardinia. Place identity (bound of place and people) is vital for reproduction of mining landscape in Sardinia as a place for living and loving. Both theory and practice, suggest territoriality of place-specific identities. The development principles focused rethinking the heritage conception on the regional level, but starting from and with the local community. Research suggests more amplification of everyday life practices for a particular site of the mining landscape in Sardinia.

Dottore di Ricerca/Ph.D.: **Giovanni Campus**

Data di Discussione della Tesi/Date of Thesis Defense: **2.3.2018**

Titolo della Tesi/Thesis Title: **"The City as Theatre: The Performing Space"**

Tutor/Adviser: **Arnaldo Cecchini**; Co-Tutor/Co-Adviser: **Zoran Đukanović**

### **Abstract**

This research aims at investigating the theoretical basis, the role, and the regularities of performing arts in the urban environment.

References to theatre and dance are abundant in urban studies, but they serve almost exclusively as metaphors. Investigating the specificity of performing arts will also allow clarifying the performative aspects of every artistic intervention in urban space.

Indeed, from ancient rituals to contemporary street theatre, an intentional and staged action plays a significant role not only in the processes of sense giving and community building, or in what is today called "placemaking," but also in the production of space.

The second section of the work, called "Atlas," while working as a repertoire of case studies supporting the theoretical text, is also intended to work autonomously by building a parallel discourse through images. That section aims to demonstrate how a range of performance interventions produce the city and underscore the notion that theatre is a requirement in the production – or building – of urban space and, as such, forms a continuum with architecture and urban design.

The thesis is completed with a section of interviews with choreographers and directors who have dedicated their attention to performance in the urban environment.

Dottore di Ricerca/Ph.D.: **Silvia Farris**

Data di Discussione della Tesi/Date of Thesis Defense: **2.3.2018**

Titolo della Tesi/Thesis Title: "**Energie rinnovabili: paesaggio, territorio e collettività locali**"

Tutor/Adviser: **Paola Pittaluga**

### **Abstract**

Securing a sustainable and reliable energy supply is one of the main topics of the environmental issues we are facing today. Energy transition to more sustainable energy systems is supposed to resolve not only the decreasing availability of fossil fuels, but also the environmental and social issues the actual energy systems entail. Renewable energy systems deal not only with economical and technical issues, but also spatial issues, which comes as implications of the low energy efficiency obtainable from the main renewable sources, that require large areas of installation. The blueprinting and implementation of sustainable patterns of life cannot overlook the territoriality they entail, and the echoes on local systems, which are tangible and quantifiable on the one hand, and intangible and elusive on the other hand. The research is aimed to understand the landscape evolution caused by the forthcoming renewable energy systems. Furthermore, consequent topic is understand how a productive energy landscape can be translated in a sustainable landscape, including the environmental and social issues here implied. Therefore, sustainable energy systems rely on a substantial local involvement, resulting in community-owned and managed energy systems, as a result of both, grassroot actions and mainstream energy policy.

Dottore di Ricerca/Ph.D.: **Omar Sosa Garcia**

Data di Discussione della Tesi/Date of Thesis Defense: **2.3.2018**

Titolo della Tesi/Thesis Title: **"Fragmentos de identidad insular. Paisaje y cultura local como instrumentos para la planificación turística de Agaete y Alghero"**

Tutor/Adviser: **Paola Pittaluga**

### **Abstract**

Lo sviluppo del turismo di massa prodotto in Spagna e Italia a partire dalla metà del XX secolo rappresenta un fondamentale impulso economico nei territori insulari quali sono Gran Canaria o la Sardegna comportando, però, anche una serie di problematiche come l'intenso processo di urbanizzazione, il degrado del paesaggio o un'eccessiva influenza sulle comunità locali. Pertanto, questo lavoro pone i valori del paesaggio e il patrimonio delle aree costiere di origine non turistica al centro di una metodologia che punta a un modello turistico nuovo e complementare per i casi studio scelti, Agaete e Alghero. Infatti, l'analisi delle logiche di costruzione del territorio e del paesaggio, la catalogazione del patrimonio storico e lo studio della storia locale, permettono la definizione di percorsi narrativi in grado di interpretare e valorizzare gli elementi che meglio rappresentano l'identità locale. Questo approccio aiuta ad estendere l'interesse turistico dalla costa verso le aree interne, riducendo i problemi derivati dall'eccessiva pressione turistica subita dalla costa e valorizzando le importanti aree agricole di entrambi i casi studio.

Dottore di Ricerca/Ph.D.: **Roberta Guido**

Data di Discussione della Tesi/Date of Thesis Defense: **2.3.2018**

Titolo della Tesi/Thesis Title: "**Diritto alla città e diritto all'ambiente urbano. Dalle pratiche alle regole**"

Tutor/Adviser: **Arnaldo Cecchini**; Co-Tutor/Co-Adviser: **Domenico D'Orsogna**

### **Abstract**

The research is driven by the motivation to contribute to the elaboration of the "science of the city" (Lefebvre), through the study of relationships and correlations which insist in the city.

The choice is to investigate processes in which the lefebvrian concept of the "right to the city" is claimed in order to verify if it can be verified in these contexts not only the emergence of rights or a way of exercising rights related to the city: above all, it intends to understand if a capacity for legal production can be identified.

Recognizing the impossibility and uselessness of denying the conflict, and even evaluating the contribution of urban movements and practices in promoting greater collective well-being, it was decided to verify their contribution to generate another meaning of the right to the city that include the genesis of rules and effective government tools.

It has been chosen to adopt a methodology strongly based on research-action (the ongoing process of Cavallerizza Reale in Turin; MiraMap in Mirafiori Sud neighborhood, the Regularment of Commons) and case-studies (in Italy, Spain, France, USA, Latin America) that allowed analysis and continuous interactions.

It was intended to operate considering the interaction between movements and groups with the institutions, in order to verify dialectics according to their contribution to the general interest, for an improvement of institutions and generative processes of norms.

**Corso di Dottorato in  
Scienze della vita e Biotecnologie**

—

**Ph.D. Program in Life Sciences and  
Biotechnologies**

Coordinatore/Coordinator: Prof. Leonardo A. Sechi

Dottori di Ricerca/Ph.D.

Marcello Abbondio

Maurizio Caocci

Bilab Djeghout

Giulia Ganau

Davide Maselli

Thi Hieu Dung Nguyen

Magdalena Niegowska-Conforti

Luca Sanna

Simona Sanna

Dottore di Ricerca/Ph.D.: **Marcello Abbondio**

Data di Discussione della Tesi/Date of Thesis Defense: **6.4.2018**

Titolo della Tesi/Thesis Title: **"Metaproteogenomic analyses of the gut microbiota in human and animal models: identification of changes induced by special diets in health and disease"**

Tutor/Adviser: **Sergio Uzzau**

### **Abstract**

Gut microbiota (GM) is known to have a role in immune system development, metabolism and protection from enteropathogen invasion. Characterizing the health-associated GM is key to formulate targeted interventions in case of dysbiotic states. As diet is one of the main factors with an impact on gut microbes, comprehending how it shapes the GM is also crucial.

In view of this, through an integrated multi-omic approach based on 16S and shotgun metagenomics and metaproteomics, several studies were performed to obtain deeply characterized GMs in human, sheep and animal models and to shed light on specifically selected diet-GM interactions.

First, the GM of a human healthy cohort and sheep were in-depth characterized, improving insights on taxonomy, active and taxon-specific functions. Further, butyrogenesis and glutamate degradation were detected as consistently active in all human subjects, becoming potential candidates for biomarkers of intestinal health.

Second, the response of GM to caloric restriction (CR), and the GM possible changes at the onset of celiac disease (CD) were evaluated in animal models. Several changes solely due to CR were noted, regarding *Lactobacillus* spp. abundance and propionogenesis, while microbiota changes clearly related to the onset of CD were not observed.

Lastly, preliminary data on two pilot studies on small human populations were reported, the first based on the analysis of different diet habits and the second as an actual dietary intervention.

Dottore di Ricerca/Ph.D.: **Maurizio Caocci**

Data di Discussione della Tesi/Date of Thesis Defense: **6.4.2018**

Titolo della Tesi/Thesis Title: **"IFN $\alpha$ -mediated suppression of JCV is mTOR pathway dependend"**

Tutor/Adviser: **Caterina Serra**; Co-Tutor/Co-Adviser: **Antonina Dolei**; **Kamel Khalili**

### **Abstract**

The severe demyelinating disease progressive multifocal leukoencephalopathy (PML) is caused by the neurotropic polyomavirus JC (JCV), which replicates in oligodendrocytes and astrocytes in the brain. Infection by JCV is very common and is widespread worldwide, but PML occurs very rarely. Primary infection occurs early in life, usually in childhood, but the virus is contained by the action of immune system and subsequently persists asymptotically. Initiation of PML occurs occasionally under conditions of immune dysfunction and results from the reactivation of persistent virus from an inactivate state to replicate lytically. Our earlier studies suggest that reactivation occurs within glial cells due to the action of cytokines, e.g. TNF-alpha, stimulating viral gene expression. In this study, we have now examined the cytokine interferon-alpha (IFN-alpha), which, in contrast, has a negative effect on JCV gene expression and replication. IFN-alpha and IFN-beta inhibited the replication of JCV in primary human fetal astrocytes and reduced transcription by JCV promoter reporter constructs in oligodendroglioma cells. We found that IFN- $\alpha$  treatment of glial cells induced expression of STAT1 and caused STAT1 phosphorylation and translocation to the nucleus. Other downstream signaling events were also examined including PI3K/Akt and mTOR and inhibition of PI3K with LY294002 was found to enhance JCV replication while rapamycin inhibition of mTOR affected STAT1 translocation to the nucleus. We conclude that pathways downstream of IFN-alpha negatively regulate JCV gene expression and replication and this may present new therapeutic opportunities for PML.

Dottore di Ricerca/Ph.D.: **Bilal Djeghout**

Data di Discussione della Tesi/Date of Thesis Defense: **6.4.2018**

Titolo della Tesi/Thesis Title: "**Diversity of Non-Typhoidal Salmonella in Algeria**"

Tutor/Adviser: **Salvatore Rubino**

### **Abstract**

Non-typhoidal Salmonella (NTS) are globally recognized as important pathogens associated with gastroenteritis. In most cases, humans are infected through consumption of contaminated food products, especially food of animal origin. In developing countries including Algeria, there is a lack of documentation, surveillance projects and initiatives. Thus, this has led to an underreporting of Salmonella serovars. The overall aim of this thesis was to identify the different Salmonella serovars isolated from human and poultry in Algeria, and to determine the prevalence of antimicrobial resistance in these isolates. Furthermore, full genome sequences of the isolates were analysed in silico for molecular characterization. Different serovars have been identified among the human isolates, naming *S. Typhimurium* as the most dominant, followed by *S. Kentucky*, *S. Enteritidis*, *S. Heidelberg*, *S. Ohio*, *S. Lindenburg*, *S. Indiana*, *S. Virchow*, and *S. Bonn*. Instead, *S. Gallinarum* was the only serovar found among the poultry isolates. The isolates displayed resistance to multiple antimicrobials. It was mediated by various genes encoding for resistance to  $\beta$ -lactam antibiotics, carbapenems, quinolones, aminoglycosides and to co-trimoxazole. Classical Salmonella genomic island 1 was identified in serovar *Typhimurium*, while new variant of SGI1 named SGI1-K7 was identified in serovar *Kentucky*. Plasmids belonging to incompatibility group FIB and FII were the most commonly identified among the isolates.

Dottore di Ricerca/Ph.D.: **Giulia Ganau**

Data di Discussione della Tesi/Date of Thesis Defense: **6.4.2018**

Titolo della Tesi/Thesis Title: "**Studio della virulenza di Staphylococcus spp isolati da protesi mammarie**"

Tutor/Adviser: **Salvatore Rubino**

### **Abstract**

In recent years the use of breast surgery, has undergone an exponential increase, both for aesthetic and reconstructive purposes. The main complication as a result of these interventions is due to the bacterial colonization of the breast implants resulting in infection of the affected site. As a result of the diagnosis of an infection, the only possible therapy involves the removal of the implant followed by antibiotic treatment. The main culprits of such infections are Staphylococcus spp. It was possible to study the pathogenicity of these strains from a genetic point of view by identifying specific virulence genes such as icaA, bhp, kdp, agrD, IS256 and IS257. Moreover, it has been studied their adhesive capacity both on epithelioid Caco2 cells and on all types of prosthetic surfaces, comparing with ATCC control samples. Their ability to produce biofilms was compared with ATCC strains, clinical control samples and skin-isolated specimens of healthy voluntary women has also been studied. The study has made it possible to broaden the knowledge of these particular infections hitherto poorly studied and to lay the basis for future interventions of prevention and advancement in the diagnostic and surgical methods.

Dottore di Ricerca/Ph.D.: **Davide Maselli**

Data di Discussione della Tesi/Date of Thesis Defense: **6.4.2018**

Titolo della Tesi/Thesis Title: **"The role of mechanical stress in progression of intima hyperplasia associated to vein coronary bypass grafts disease"**

Tutor/Adviser: **Gianfranco Pintus**

### **Abstract**

Coronary artery bypass grafting is a surgical procedure introduced to restore the blood circulation into the myocardium after an ischemic event. Despite progress in the use of arterial conduits, saphenous vein (SV) remains one of the most used vessels for the bypass. A short time after bypass implantation SV undergoes intima hyperplasia (IH) that progressively reduce its patency. One trigger cause of IH is the hemodynamic changes in the blood flow with higher shear stress on the endothelial layer a radial deformation on the wall of the vein.

The aim of this project was to understand the role of saphenous vein progenitors (SVP) in the progression of IH. These cells with high differentiation potential are the pericytes of vasa vasorum in the tunica adventitia.

By in vitro and ex vivo models of mechanical stress we demonstrated the susceptibility of SVPs to the strain that causes a cytoskeletal reorganization and the acquisition of a potential migratory phenotype. SVPs showed the stimulus-related up-regulation of Amphoterin-Induced Gene And Open Reading Frame 2 (AMIGO2), that may have a role in the mechanical activation via prosurvival and migratory effects.

For the first time has been described the presence of AMIGO2 in SVPs and its relationship with mechanical stress. Migratory phenotype acquisition and AMIGO2 overexpression demonstrate how SVPs are potential targets for further study of IH.

Dottore di Ricerca/Ph.D.: **Thi Hieu Dung Nguyen**

Data di Discussione della Tesi/Date of Thesis Defense: **6.4.2018**

Titolo della Tesi/Thesis Title: **"Dose-dependent effect of Resveratrol on human endothelial cell functions"**

Tutor/Adviser: **Gianfranco Pintus**

### **Abstract**

Purpose - Resveratrol consumption has been shown to exhibit cardiovascular-preventive and anticancer activities in preclinical studies. The mechanism of Resveratrol effect on human umbilical vein endothelial cell proliferation and apoptosis were not clearly understood. This study was undertaken to study on the dose-dependent effect of Resveratrol on HUVEC function and identify the potential signals involved in this pathway.

Experimental Design and Results - HUVECs were used as described in this study. Treatment of HUVECs with the concentrations of 1 and 100  $\mu$ M RES showed that low concentrations increase cell growth, and decrease intracellular ROS levels while high concentrations cause the opposite effect significantly. The result of DNA fragmentation experiments may indicate cell death by apoptosis in HUVECs related to the expression of Bax and the decrease of the expression of Bcl-2. Using RES 50  $\mu$ M, is consistent with the significant increase in DNA fragmentation, a typical marker of apoptosis. And at this concentration, RES makes endothelial cell cycle arrest by reducing Cyclin D1 and ODC, c-myc expression. Resveratrol dose-dependently modulates PKC activity on HUVEC proliferation and apoptosis.

Conclusion - Our data indicated that the RES effect on HUVECs is biphasic. PKC appears to be the potential mediator of the observed Resveratrol effect on HUVEC functions (proliferation, apoptosis), hypothesized this linked to the intracellular ROS levels.

Dottore di Ricerca/Ph.D.: **Magdalena Niegowska-Conforti**

Data di Discussione della Tesi/Date of Thesis Defense: **6.4.2018**

Titolo della Tesi/Thesis Title: "**Immunogenicity of *Mycobacterium avium* subsp. *paratuberculosis* epitopes cross-reacting with human ZnT8 and proinsulin peptides in autoimmune diabetes**"

Tutor/Adviser: **Leonardo A. Sechi**

### **Abstract**

Although numerous studies put in evidence the increasing incidence of type 1 diabetes (T1D), its cause remains unclear. The role of *Mycobacterium avium* subsp. *paratuberculosis* (MAP) as a putative environmental agent triggering or accelerating the disease has been previously hypothesized in Sardinian and Italian T1D populations. The present thesis further sustains this association by reporting an elevated seroreactivity to MAP-derived epitopes and homologous human peptides corresponding to proinsulin and ZnT8 fragments in populations at different T1D stages and originating from distinct biogeographic backgrounds. Anti-MAP antibodies (Abs) resulted detectable in the first months of life before the appearance of classical autoantigens and, in most cases, were maintained in time making the selected peptides good candidates for early biomarkers. Likewise, Abs responses to the same antigens were observed among LADA patients and subjects affected by Hashimoto's thyroiditis which frequently complicates T1D. Validation with a MAP-specific lipopentapeptide confirmed these results in coincidence with a stable Abs status. In PBMC primary culture, ZnT8 peptide and its MAP homolog induced the expression of proinflammatory cytokines along with increased cell-mediated responses and apoptosis. Good correlation between values obtained for the homologous MAP/human peptide pairs point at cross-reactivity through which mechanisms of self tolerance may be disrupted leading to autoimmunity.

Dottore di Ricerca/Ph.D.: **Luca Sanna**

Data di Discussione della Tesi/Date of Thesis Defense: **6.4.2018**

Titolo della Tesi/Thesis Title: **"Antiproliferative activity of Verteporfin in Embryonal and Alveolar Rhabdomyosarcoma cell lines"**

Tutor/Adviser: **Luigi Marco Bagella**

### **Abstract**

Rhabdomyosarcoma (RMS) is a pediatric tumor, which arises from muscle precursor cells. Recently, it has been demonstrated that Hippo Pathway (Hpo) is involved in tumorigenesis of RMS. Thanks to its kinase cascade, which activates Yes-Associated Protein 1 (YAP1-YAP) and transcriptional co-activator with PDZ-binding motif (TAZ), Hpo is able to activate several physiological and biological features. YAP and TAZ are the heart of Hpo and they showed to have both cytoplasmic and nuclear role. In the nucleus, YAP is able to bind TEAD factors and constitute a complex that activates the transcription of several genes such as MYC, Tbx5 and PAX8 or maintains the stability of others like p73.

The key role of YAP and TAZ in cancer is leading to the development of new compounds able to block their action. One of these drugs is called Verteporfin (VP). This molecule is able to stop the formation of YAP/TEAD complex in the nucleus.

Considering that RMS is an aggressive tumor and that YAP recovers an important role on it, the aim of this project was to understand if VP is able to have a specific effect on RMS cell lines.

This work showed that VP has an antiproliferative action on RMS cell lines. VP perturbs cell cycle in a different manner depending on RMS cell lines. Through its action, VP modifies also the phenotype of RMS cells. Moreover, this drug is able to induce the activation of apoptosis mechanism through the cleavage of PARP protein in RMS cell lines. Furthermore, siRNA-induced knock down of YAP clarifies that VP induces anti proliferative action through other mechanism.

Dottore di Ricerca/Ph.D.: **Simona Sanna**

Data di Discussione della Tesi/Date of Thesis Defense: **6.4.2018**

Titolo della Tesi/Thesis Title: "**Epigenetics and neurodegeneration: physiological relevance of TDP-43/HDAC1 interaction**"

Tutor/Adviser: **Claudia Crosio**

### **Abstract**

TDP-43 pathology is a disease hallmark that characterizes both sporadic and familial amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD-TDP). TDP-43 has been implicated in transcription, RNA metabolism and transport, and different TDP-43 post-translational modifications, spanning from phosphorylation to acetylation, can regulate its activity. In the present PhD thesis we provide evidences that TDP-43 interacts with histone deacetylase 1 (HDAC1), both in vivo and in vitro. By biochemical assays, performed in SH-SY5Y cells, we demonstrated that HDAC1, as well as HDAC6, can modify TDP-43 acetylation, that occurs mainly on amino acid residues K142 and K192, located in the RRM1 and RRM2 domains, necessary for the interaction. Interestingly, HDAC1 overexpression modulates TDP-43 transcriptional activity on CHOP promoter, but not TDP43 splicing activity on polymerase delta interacting protein 3 [POLDIP3] gene. Finally, both in cell culture and in Drosophila, HDCA1 reduced level (genomic inactivation or siRNA) or treatment with pan-HDAC inhibitors, reduce WT or pathological mutant TDP-43 toxicity, suggesting TDP-43 acetylation as a new potential therapeutic target.

Corso di Dottorato in  
Lingue, Letterature e Culture dell'età  
moderna e contemporanea

-

Ph.D. Program in  
Languages, Literatures and Cultures of the  
modern and contemporary age

Coordinatore/Coordinator: Prof. Massimo Onofri

Dottori di Ricerca/Ph.D.

Giuseppe Bianco

Silvia Carrus

Valentina Chiocchia

Katia Deiana

Gavino Balata

Maria Teresa Antonia Morelli

Giannella Biddau

Gabriele Tanda

Federico Valenti

Stefania Zanda

Dottore di Ricerca/Ph.D.: **Giuseppe Bianco**

Data di Discussione della Tesi/Date of Thesis Defense: **20.3.2018**

Titolo della Tesi/Thesis Title: **"Rappresentazione di cartografia storica della città di Sassari in ambiente GIS Open Source. "**

Tutor/Adviser: **Gavino Mariotti**

### **Abstract**

The aim of this research is to evaluate a methodology for the analysis of historical maps by applying open source GIS software.

Maps of "Città di Sassari" has been first collected, then, after proper editing using a graphic software, processed by a GIS (Geographic Information System). By comparing those systems with updated new maps has been possible to get final results. The cartography used is the one of "Città di Sassari" currently known. Both measured and derived maps were have been used. The former obtained through measurements and surveys performed on the ground by topographers while the latter through a series of re-elaborations performed by cartographers. As regards historical cartography we wanted to understand what was detected with elementary topographic tools, even before the advent of aerophotogrammetric technique. Before entering into the real GIS, are presented those that are the basic maps that represent Sardinia, as well as a list, with related description, of the main detectors / cartographers and maps of Sassari. The feasibility of employing an Open source software has been also part of the research except for the IT tools of office automation.

The reason of such decision could be addressed almost exclusively by economic reasons, because studies about historical cartography are conducted mainly in academic fields, where, unfortunately, is almost lack of funds. The research has had positive results, showing that free software can be used without reservations.

Dottore di Ricerca/Ph.D.: **Silvia Carrus**

Data di Discussione della Tesi/Date of Thesis Defense: **20.3.2018**

Titolo della Tesi/Thesis Title: **"Potenziamento del settore turistico sardo attraverso la valorizzazione delle risorse locali mediante sistemi di *mobile marketing* e codici QR"**

Tutor/Adviser: **Gavino Mariotti** Co-Tutor/Co-Adviser: **Maria Veronica Camerada**

### **Abstract**

The study focuses on the reciprocal relationship between spaces and the creation process of the territorial value, identifying the routes by which to increase the attractiveness of the places in order to augment their competitive profile. The research identifies the "authentic and high quality" tourism demanded by both national and international tourists and applies an analysis model which looks at the competitiveness of the destination based on the territories environmental and cultural resources. The elements enable the places to be defined and we can then consider the new ways of travelling and the corresponding segments of the market to which the Strategies of Tourism Destination Development should be directed. The research develops and applies an analysis model of the Customer Experience that examines tourists in the Internet age, through face-to-face interviews with 300 travellers, Content Analysis on almost 1,000 reviews and the popularity of search terms on Google Trends, providing a clear picture on the needs of tourists. The results of the survey allow us to define a tool for territorial development, called FoodExplorer, based on a digital information system to support the enhancement of the Sardinian tourism sector. The service is designed for the 2.0 tourist who appreciates the quality of the local products and, through a smartphone and a mobile marketing system mediated by QR code, is incentivized to discovery and learn about the territory.

Dottore di Ricerca/Ph.D.: **Valentina Chioccia**

Data di Discussione della Tesi/Date of Thesis Defense: **20.3.2018**

Titolo della Tesi/Thesis Title: "***Volan ausel' per air di straine guise: gli animali come immagini del fare poetico nella poesia del Duecento e in Dante***"

Tutor/Adviser: **Monica Farnetti**

### **Abstract**

The present work focuses on the observation and the study of animal figures as metapoetical meanings that we find in the similies, the metaphors and the transumptiones of the Italian poetry of the XIII century and in Dante's corpus. Starting from the XII century, indeed, animals began to appear in the Romanic lyric production as metaphors of rhetorical, stylistic and poetical conceptions. Trough animal images, poets could express either their ideas about poetry or about the compositive methods of other writers or even about the rules of a particular literary genre. Considering the interpretative categories of Medieval zoological symbolism, the analysis of the specifical occurrences and of the intertextual relations interowen trough these animal figures, the author provides a wide range of the meanings of a specific animal image and of its metaliteral implications. The section "For a metaliteral bestiary" presents and gives a syntetical comment on the most common animal figures of the Italian poetry of the XIII century: the hypernym of bird, the swan, the nightingale, the crow and the lark. The section "Metapoetical animals in the Commedia", on the other hand, focuses on the interpretation of the metapoetical animal figures present in Dante's poem such as the hen, the snake, the starling, the crane, the dove and the eagle.

Dottore di Ricerca/Ph.D.: **Katia Deiana**

Data di Discussione della Tesi/Date of Thesis Defense: **20.3.2018**

Titolo della Tesi/Thesis Title: **"Experimental phenomenology on the role of chromatic accentuation in reading tasks"**

Tutor/Adviser: **Baingio Pinna**

### **Abstract**

According to Gestalt psychologists, color is considered a secondary attribute and a less effective tool if compared to shape, luminance and motion. In this work novel and meaningful visual properties given by chromatic variations in the reading process in normal and dyslexic readers have been studied. It was shown that color highlights wholeness, parts-whole organization and phenomenal fragmentation during reading and comprehension tasks in reading texts made of words and non-words modified through several color conditions: monochromatic (the whole text colored with only one color); word (each word colored in different color); half word (half word colored in a color different from the one of the second half); syllable (every syllable in a different color); letter (each letter in a different color). The aleatory variables here considered were: the reading time, the reading errors and the incorrect answers given in a comprehension test. The outcomes demonstrated that these variables are all directly related and strongly affected by the five chromatic conditions. These findings illustrate similar trends in the four groups of readers: children and adults, normal and dyslexic readers. Further possible researches and eventually some clinical applications are also discussed along with some questions related to color vision. They suggest the main purposes of color for living beings which is that to generate wholeness, parts-whole organization and perceptual fragmentation.

Dottore di Ricerca/Ph.D.: **Gavino Balata**

Data di Discussione della Tesi/Date of Thesis Defense: **20.3.2018**

Titolo della Tesi/Thesis Title: **"Innovazione e crescita nell'industria creativa e culturale: il ruolo delle start-up per il trasferimento tecnologico"**

Tutor/Adviser: **Gavino Mariotti**; Co-Tutor/Co-Adviser: **Alessio Tola**

### **Abstract**

The goal of this work is the analysis of the technological trends of the Creative and Cultural Industries (CCI). To define the field of study of the thesis, the work carried out by the European Commission was taken as a starting point. The study focused on the projects carried out by researchers in some sectors of application of ICT in the CCIs. Starting from the innovative push promoted by the R&D support tools and from the results obtained from the projects, we started to analyse the operations of the cultural operators working in the ICC sector. The result of this first effort was used to build a pilot questionnaire which had the objective of highlighting the innovative behaviour of Sardinian cultural operators. The second part of the work has maintained an experimental approach during which a qualitative and quantitative study was carried out on the start-up population active in the ICC sector in Italy. The aim of the study was to verify the CCI start-ups' operating conditions, performances, technological assets, entrepreneurial attitudes, the type of activity and, ultimately, the salient features. The objective of this analysis is to identify operational patterns and factors related to the managerial style, financial and technological aspects capable to help identifying successful models in this sector.

Dottore di Ricerca/Ph.D.: **Maria Teresa Antonia Morelli**

Data di Discussione della Tesi/Date of Thesis Defense: **20.3.2018**

Titolo della Tesi/Thesis Title: **"Il Rotary International e il Distretto 2080: una storia istituzionale: con un'appendice sul Rotary e la promozione della cultura musicale"**

Tutor/Adviser:**Giampaolo Mele**; Co-Tutor/Co-Adviser: **Angelo Aldo Castellaccio**

### **Abstract**

On February 23rd, 1905, the constitutive meeting of the first Rotary Club took place in Chicago. In 1922, at the Los Angeles convention, the National Association of Rotary clubs became the International Association of Rotary club, later shorten in the current Rotary International.

In 1945, Rotary is invited to participate at the foundation of the United Nations and still today is consultative member of numerous supranational bodies. The first Italian Club was founded in Milan in 1923; because of the strong contrasts with the fascist regime in 1938, the Italian Rotary clubs dissolved to rebuild themselves in the aftermath of the Second World War, starting from the South, from Sicily, following the stages of Liberation.

Rotary also has a conflicting relationship with ecclesiastical institutions, concerned by the growing development and dissemination of Rotary at international level. This research pays particular attention to the Rotary Foundation, whose centenary occurred in 2017, to the admission of women to Rotary and to the ceremonial where hymns featured prominently.

Dottore di Ricerca/Ph.D.: **Giannella Biddau**

Data di Discussione della Tesi/Date of Thesis Defense: **23.10.2018**

Titolo della Tesi/Thesis Title: **"Costruttivismo ed esperienzialismo per l'apprendimento dell'italiano L2 nelle visite museali"**

Tutor/Adviser:**Johanna Monti**

### **Abstract**

The present PhD thesis evolves from the need to grow awareness of the didactic methods that could be adopted in the field of the acquisition of Italian as a second language, and that could contemporaneously be optimal instruments to give value to museums and to consider them as ideal learning settings. Therefore, the aim of my research is, first of all, to show the dynamics of the acquisition in museums. Afterwards, I make an excursus into the theories postulated by scientists who (has) studied and supported Constructivism and Experiential Learning. Moreover, I explain how to reify scientists' thought and I focus on two Sardinian museums: Museo del corallo in Alghero and Museo-Casa di Grazia Deledda in Nuoro. On these two structures I have constructed *ad hoc* two didactic paths consisting of different steps and also including materials whose objective is to allow students to intimately dialogue with the exposed items in order them to learn Italian language and culture. The working sheets are accompanied by the analysis of the activities from the Constructivist and the Experientialist perspectives. Ultimately, to confirm the functionality and the value of the two approaches, I present the results of an experiment conducted in the Museo del corallo with a group of Erasmus students hosted by the University of Sassari, highlighting the strong points and providing conclusive considerations for eventual future executions of the initiative.

Dottore di Ricerca/Ph.D.: **Gabriele Tanda**

Data di Discussione della Tesi/Date of Thesis Defense: **23.10.2018**

Titolo della Tesi/Thesis Title: **"Un riso che si rinnova: nuovi strumenti critici per l'umorismo dopo Pirandello (discussione in lingua italiana)"**

Tutor/Adviser:**Marco Manotta**; Co-Tutor/Co-Adviser:**Massimo Onofri**

### **Abstract**

In contemporary Italian literature the study of humor is not systematic and often uses old theories such as those of Bachtin and Bergson. In this PhD thesis I try to widen the method to other disciplines and to set up a Canon that starts from Pirandello up until the nineties. As a result, the theoretical part connects anthropological, neuroscientific, cognitive linguistics and cultural history studies. The aim is to set up a ductile method that gives the possibility to evaluate different angles of humor and, at the same time, to offer a valid support to the study of the humorous text in its historical dimension. The choice of the writers that were examined builds a small reference Canon of this literary genre in Italy that does not evaluate only the artistic value, but also the public diffusion. Since humor is a genre very influenced by the historical moment and the mentality, this study also deepens the events and the historical context in which the narrative works are written.

Dottore di Ricerca/Ph.D.: **Federico Valenti**

Data di Discussione della Tesi/Date of Thesis Defense: **23.10.2018**

Titolo della Tesi/Thesis Title: "**Biological Classification in Early Chinese Dictionaries and Glossaries: from Fish to Invertebrates and Vice Versa**"

Tutor/Adviser:**Elisa Levi Sabattini**

### **Abstract**

This dissertation problematises the classification of chong 蟲 (invertebrates) and yu 魚 (fish) in Early Chinese texts. The loci classici analysed will range from the Warring States (ca. 453 – 221 BCE) to the Eastern Han period (dong Han 東漢, 25 – 220 CE). The focus is on the lexical ambiguity between these two zoological categories: despite being perceived as different, they include a more or less loose set of “dynamic” words that shift from one category to the other. The project concentrates on two early Chinese texts: the Erya 爾雅 (III century BCE) and the Shuowen jiezi 說文解字 (100 CE). These works had a pivotal role during the development of Chinese lexicography and gave the lexical basis of later texts. They are also the first texts that deal with the problem of taxonomical classification in Early China. By systematically applying a philological approach (Coblin 1972, Carr 1979) to a selection of zoological glosses preserved in these sources, this study aims at reformulating the way in which early Chinese “protozoological categories” are organised (Needham 1986, Sterckx 2002). Through the analysis of selected case studies, it aims at showing that even if there are fairly well attested categories that constitute a dichotomous system (such as “quadrupeds” versus “winged creatures” or “wild beasts” versus “domestic animals”), Early Chinese taxonomies represent a dynamic and unstable attempt at zoological classification for what we call today “fish” and “invertebrates”.

Dottore di Ricerca/Ph.D.: **Stefania Zanda**

Data di Discussione della Tesi/Date of Thesis Defense: **23.10.2018**

Titolo della Tesi/Thesis Title: "**Il punto cieco del diritto: a proposito di Salvatore Satta e Salvatore Mannuzzu** "

Tutor/Adviser:**Massimo Onofri**; Co-Tutor/Co-Adviser: **Aldo Maria Morace**

### **Abstract**

The Law is in crisis because it can no longer find a common ground. Economics, media and political power try to influence it. This is why the laws risk to move away from the needs of the people. For this reason some scholars have begun to approach the study of law using literature. The aim of this PhD dissertation is to create a taxonomy of the different approaches of the Law & Literature method, with particular attention to the ethical setting of academics such as François Ost and Martha Nussbaum. After this theoretical introduction, the study continues with the analysis of the works of two Sardinian writers: Salvatore Satta and Salvatore Mannuzzu. Both of them were writers and jurists. It was important to deepen their narrative works in light of their legal convictions. Satta was in fact a refined theoretician of law, one among the influential scholars of the civil trial and also the author of one of the greatest books of Italian literature of the twentieth century, *Il giorno del giudizio* (*The Day of Judgment*). Mannuzzu was a judge involved in the daily life of the trial; he presided over government investigations and was also a prolific writer. Are the interactions between the two vocations useful for better understanding justice and their literature?

**Corso di Dottorato in  
Scienze Agrarie**

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**Ph.D. Program in Agricultural Sciences**

Coordinatore/Coordinator: Prof. Ignazio Floris

Dottori di Ricerca/Ph.D.

Curriculum Agrometeorologia ed ecofisiologia dei sistemi agrari e  
forestali

Andrea Cantore Badurina

Pierfrancesco Deiana

Dottore di Ricerca/Ph.D.: **Andrea Cantore Badurina**

Data di Discussione della Tesi/Date of Thesis Defense: **14.2.2018**

Titolo della Tesi/Thesis Title: **"Influenza delle condizioni pedoclimatiche sulla selezione di caratteri funzionali nella struttura anatomica di *Olea europaea*"**

Tutor/Adviser:**Maurizio Mulas**

### **Abstract**

The olive tree (*Olea europaea* L.) spread from Near-East to western Mediterranean basin and cultivated varieties were multilocally selected. Morphological traits, which could have been adapted to the climate condition, could have been later influenced by human selection. Several morphological traits of wild-type and olive cultivar trees were analysed to understand which traits have been influenced by human selection. Those traits that showed significative differences have been correlated to climate data to understand how climate influenced wild olive morphology. Strong correlation has been observed among leaf traits and among ramification traits, but those were not strongly correlated to climate data. Principal component analysis shows that some components could explain a large percentage of variance. Multiple regressions show which climate data seem to be more effective in explaining wild olive morphology differences. Some climate data seem to explain differences in wild olive morphology, but wider studies on a bigger collection are needed to better understand the effect of climate on olive characters.

Dottore di Ricerca/Ph.D.: **Pierfrancesco Deiana**

Data di Discussione della Tesi/Date of Thesis Defense: **14.2.2018**

Titolo della Tesi/Thesis Title: **"Phenology and characterization of virgin olive oils from admitted to PDO "Sardegna", minor Sardinian and international varieties"**

Tutor/Adviser:**Maurizio Mulas**

### **Abstract**

Global virgin olive oil (VOO) production and consumption constantly increased during last 20 years. The expansion of growing areas in southern Mediterranean and in new countries, together with the enhancement of growing techniques, has led a reduction of production costs, maximizing productivity. Interest on the high quality and the nutraceutic properties of VOO is rising.

The wide biodiversity of Italian olive germplasm is an important resource for improve quality, differentiate and promote specific productions.

The aim of this thesis is to improve the knowledge of the Sardinian olive germplasm, with a particular focus on those varieties that characterize PDO "Sardegna", trying to identify the ones that might contribute better to improve label's quality.

In a three years field test, phenological behavior and interaction with meteorological conditions of 26 local and national varieties were evaluated. Corresponding olives samples were processed and monovarietal VOO were analyzed. The influence of harvest period on the VOO quality of 3 Sardinian varieties was studied. Similar environmental, agronomic and extraction conditions were maintained. The study of phenological behavior and VOO composition revealed some peculiar qualitative aspects, specific of some varieties. Moreover, genetic factor affected fruit ripening process. Further studies might help to evaluate better the potentialities and valorization of minor varieties.

Dottori di Ricerca/Ph.D.

Curriculum Biotecnologie microbiche agroalimentari

Roberto Cabizza

Maria Grazia Farbo

Angela Scanu

Dottore di Ricerca/Ph.D.: **Roberto Cabizza**

Data di Discussione della Tesi/Date of Thesis Defense: **19.2.2018**

Titolo della Tesi/Thesis Title: "**Oxytetracycline residues from spiked ovine milk to cheese: technological implications** "

Tutor/Adviser:**Pietro Paolo Urgeghe**

### **Abstract**

Antibiotics are used in livestock, in order to ensure the health of producing-food animals. Their wide use can cause an undesirable presence of residues in milk and milk products, representing a risk for human health. To guarantee the safety of consumers, the Commission Regulation (EU) 37/2010 states the Maximum Residue Limit (MRL) of pharmacologically active substances in foodstuffs of animal origin, included milk, but no limits are specified for cheese. In addition, residues in milk can have negative technological effects during the manufacturing of dairy products. Oxytetracycline (OTC) is one of the most used veterinary antibiotics in Sardinia, due to its effectiveness and low cost. The aim of this PhD thesis was to study the distribution, between cheese and whey, of OTC added in ovine milk at MRL level, and to verify technological effects during the cheese-making process. The first part of thesis was a preliminary investigation conducted by lab cheese-making method. In the second part were conducted experimental cheese-makings from whole raw milk spiked at MRL level, to understand the partition of molecule and to evaluate technological effects during the manufacturing and ripening. In the third and fourth parts were performed experimental cheese-makings from whole thermised milk spiked at half and MRL levels, to assess the influence of the thermisation on the recovery and partition of OTC, and to understand the effect of residues on the starter culture development.

Dottore di Ricerca/Ph.D.: **Maria Grazia Farbo**

Data di Discussione della Tesi/Date of Thesis Defense: **19.2.2018**

Titolo della Tesi/Thesis Title: **"Approcci eco-sostenibili per il controllo della contaminazione di ocratossina in alimenti destinati al consumo umano e animale"**

Tutor/Adviser:**Quirico Migheli**; Co-Tutor/Co-Adviser: **Barbara Sherm**

### **Abstract**

Mycotoxins are secondary metabolites produced by some filamentous fungi under certain conditions. The most important fungal genera producing mycotoxins that are found in food products are *Aspergillus*, *Fusarium*, *Alternaria*, and *Penicillium*. Ochratoxin A (OTA) has hepatotoxic, teratogenic, nephrotoxic and carcinogenic effect in mammals and it is classified as a group 2B carcinogen by the World Health Organization. The European Union has set the maximum OTA level at 2 µg/kg in wine, grape juice, and at 3 µg/kg for all products derived from cereal, including cereal products and cereal grains for human consumption. Some species of *Aspergillus* are the main source of OTA in warm and tropical regions, and in particular, *Aspergillus carbonarius* (Bainier) Thom is considered one of the most relevant OTA producers in food and feed. Hence, there is a need to develop alternative methods for pathogenic fungi and food contaminant control that will either individually or synergistically eradicate the OTA-producing fungi, by preventing mycotoxin biosynthesis, inactivating mycotoxins, or breaking them down into less or non-toxic compounds. Inhibiting the growth of OTA-producing fungi on sensitive commodities is by far the most reliable method to prevent OTA contamination of food and feed. Moreover, yeasts antagonists were evaluated able to reduce the spread of ochratoxin-producing fungi, as well as to represent the basis for biological tools to remove traces of mycotoxin from food and feed.

Dottore di Ricerca/Ph.D.: **Angela Scanu**

Data di Discussione della Tesi/Date of Thesis Defense: **19.2.2018**

Titolo della Tesi/Thesis Title: **"Studio dell'influenza di ingredienti alternativi utilizzati nel passato per il miglioramento qualitativo dei prodotti gluten-free"**

Tutor/Adviser:**Antonio Piga**; Co-Tutor/Co-Adviser: **Costantino Fadda**

### **Abstract**

In the last years the number of the celiac people is notably increased, resulting in expansion demand of gluten-free products. A strict adherence to a gluten-free diet throughout a patient's lifetime is the only possible remedy at present, as no therapy is available. Nevertheless, gluten-free foods are characterized by poor quality and a high glycemic index. The aim of this work was to develop a gluten-free bread using honey as a partial or total substitute for sucrose to reduce glycemic index and at the same time increase the antioxidant activity, due to the presence of polyphenols in honey.

Nine different formulations were produced, varying both the total sugar concentration and the percentage of sugar-honey replacement, accounting for a total sugar concentration of 9% based on flour, in order to evaluate the impact of both factors and their interaction on technological, nutritional and sensory properties.

Results showed that the increase of sugar concentration at the minimum level allowed to obtain an improvement of some quality indicators of the bread such as specific volume, colour and mechanical properties compared to the replacement. A 50% substitution of sucrose with honey improved the viscosimetric properties and cells distribution. Sensorial analysis on the consumer showed that honey improved sensory properties of bread. In general, at the 50 % replacement honey improved gluten-free bread properties.

Dottori di Ricerca/Ph.D.

Curriculum Monitoraggio e controllo degli ecosistemi agrari e forestali  
in ambiente mediterraneo

Vanessa Lozano

Gabriele Moro

Giovanni Ragaglia

Dottore di Ricerca/Ph.D.: **Vanessa Lozano**

Data di Discussione della Tesi/Date of Thesis Defense: **19.2.2018**

Titolo della Tesi/Thesis Title: **"Invasive alien aquatic plants in South American inland waters: Inventory, prioritisation and distribution models"**

Tutor/Adviser: **Giuseppe A.D. Brundu**

### **Abstract**

Biological invasions are a widespread process at the global level and can alter population dynamics, community structure and ecosystem services in the invaded range. Aquatic plants are very often particularly invasive, especially in areas that are modified by humans.

Taking into consideration the little information available, it was considered essential to plan an inventory of South American native and non-native aquatic plant species, aiming to collect information on their status of invasion, identifying the major current and the potential future plant invaders. To this aim, all the available information was collected from literature, the GBIF database and according to expert opinion. To evaluate the invasiveness of a group of aquatic plant species in South America, a standard risk assessment scheme (USAqWRA) was applied. Finally, the inventory data was used to apply a model to assess the current potential distribution of South American invasive aquatic plants. As it can be expected, considering the large number of species and diverse habitats of the investigated Continent, despite the progress herewith presented, many fundamental questions in biological invasions in South American inland waters remain unresolved. However. For this reason, I think that the opportunity provided by establishing "Global Networks for Invasion Science" are a very powerful approach with plenty of benefits, increasing the capacity to identify and assess emerging invasion risks and global trends.

Dottore di Ricerca/Ph.D.: **Gabriele Moro**

Data di Discussione della Tesi/Date of Thesis Defense: **19.2.2018**

Titolo della Tesi/Thesis Title: **"Studio del ruolo dell'effettore fitoplasmatico SAP11 nelle interazioni pianta-fitoplasma-vettore"**

Tutor/Adviser: **Vanda Assunta Prota**

### **Abstract**

Phytoplasmas are insect-transmitted Prokariotes associated with several plant diseases. They are responsible for significant economic losses in several crops and are mainly spread through infected plant material and by insect vectors. The latter, during their feeding activity, acquire the pathogen from infected plants and then transmit it, after a latency period, to new healthy plants. This process has been considered as having a passive nature for a long time but a growing body of evidences suggests that Phytoplasmas are able to actively modulate this process. Indeed, they interact with plant metabolism and negatively affect defense response against insects. This thesis presents work done to identify the nature of this interaction and especially the component explained by the effector SAP11, a protein molecule secreted into plant by Phytoplasmas during pathogenic process and involved in plant-insect interaction. Previous studies have shown that SAP11 is able to manipulate plant metabolism, causing various developmental changes and contributing to show typical symptoms associated with the presence of Phytoplasmas. Additionally, SAP11 reduces plant defense response to insect vectors, allowing them to lay more eggs and to produce more nymphs. In this paper, the role of this effector in the Phytoplasma pathogenic process is analyzed, allowing to elucidate several fundamental points of this complex plant-pathogen-insect interaction.

Dottore di Ricerca/Ph.D.: **Giovanni Ragaglia**

Data di Discussione della Tesi/Date of Thesis Defense: **19.2.2018**

Titolo della Tesi/Thesis Title: "**Studi sulla diversità della comunità batterica associata alla simbiosi ectomicorrizica tra *Tuber borchii* e *Quercus ilex* in differenti ecosistemi forestali della Sardegna**"

Tutor/Adviser: **Antonio Franceschini**; Co-Tutor/Co-Adviser: **Enrico Lancellotti, Raffaele Marongiu**

### **Abstract**

The bacterial component of the soil and of the ascocarps of the *Tuber borchii* sampled in two holm oaks grown on soils with different rock matrix was detected, in order to evaluate any quantitative-qualitative differences between the sampling sites. The chemical analysis carried out on soils samples have highlighted their main physics and chemical characteristics. The microbial communities extracted from the different soil samples were assessed both taxonomically, by sequencing the rRNA of the ribosomal 16S region of 184 bacterial isolates, and on a functional basis with the use of Ecoplates Biolog®. The microbial communities related to the ascocarp micro-habitat were evaluated with GEN III Biolog® system (36 isolates). The study has shown how the two microbial communities of the soil of the two sites, even if they are different by taxonomic composition, are identical from a metabolic-functional point of view. In addition, differences in the composition of bacterial communities are observed: among the fruiting bodies sampled by the two sites, between ascocarp and ascocarpic soil and between ascocarp and forest soil, thus corroborating the hypothesis that every micro-environment detected in this study is an ecological niche that selects specific bacterial communities. PGPR, saprophytes, fungi and human pathogens were detected among the bacteria detected in the various ascocarps.

Dottori di Ricerca/Ph.D.

Curriculum Produttività delle piante coltivate

Paolo Capece

Maria Teresa Tiloca

Dottore di Ricerca/Ph.D.: **Paolo Capece**

Data di Discussione della Tesi/Date of Thesis Defense: **21.2.2018**

Titolo della Tesi/Thesis Title: **"The Modification of rural vineyards landscapes: agroclimatic and phenological analysis in relation to possible climate change"**

Tutor/Adviser: **Giovanni Nieddu**

### **Abstract**

The purpose of this thesis is to evaluate the effectiveness of the thermal time descriptor Normal Heat Hours (NHH), in a climate change context, applied to the description of the viticultural systems based on the close relationship between thermal resources and plant phenology. In particular the research studies the way in which NHH has changed over time and the potential future changes due to climate of the vine in Sardinia over the next thirty years regarding cultivation and consequently concerning modification of the rural landscape. Recent studies show that models using NHH perform better than Degree-Day models, for all statistical indices tested and the dependent variables. Experimenting with different application methods of analysis, testing different thresholds, the thesis conducts a specific case study in region Nurra in order to generate maps of the region by applying an appropriate geo-statistical methodology and local phenological datas for many cultivars. The maps of meteorological data (i.e. temperatures, rainfalls), agro-meteorological indices (Huglin, Fregoni) and Normal Heat Hours with different thresholds permit to understand how indices varied across the territory. Moreover the thesis simulates what may happen in 2050 for the wine sector in Sardinia applying a range of climate change scenarios developed by Goddard Institute for Space Studies, GISS and the 'Hadley Center of the UK Meteorological Office.

Dottore di Ricerca/Ph.D.: **Maria Teresa Tiloca**

Data di Discussione della Tesi/Date of Thesis Defense: **21.2.2018**

Titolo della Tesi/Thesis Title: **"Soil organic carbon dynamics and land use change assessment in a no-food mediterranean cropping system"**

Tutor/Adviser: **Luigi Ledda**

### **Abstract**

The understanding of soil carbon dynamics in perennial energy systems is crucial to maintain soil fertility and agro-ecosystem sustainability. The research aims to assess the performances of five agricultural managements on soil organic carbon dynamics in a Mediterranean cropping system of cardoon (LW and HI low and high rate of N fertilizer, LW-B: plus biochar; LW-C: plus cover crop and LW-CB: plus cover crop and biochar). In addition, the impacts in terms of Land Use Change (LUC) due to conversion from biannual (barley to field bean) to cardoon were evaluated. The study was conducted from 2014 to 2017. Soil parameters of Soil Organic Carbon (SOC) content and stock were determined. Furthermore, soil respiration, temperature and moisture were monitored weekly. The best performance was showed by LW-B and LW-C managements since the biochar incorporation provided an important stable C resource that might foster C sequestration contributing to climate change mitigation. N-fixing cover crop use (i.e. subterranean clover) in perennial energy systems might be a successful strategy in terms of soil fertility enhancing and consequently ecosystem services supply. LUC and agricultural management also influenced C dynamics. The conversion of food/feed cropping system to energy one can produced a C stock increase in the soil throughout the entire perennial crop cycle that might be an useful strategy in terms of climate change mitigation.

Dottori di Ricerca/Ph.D.

Curriculum Scienze e tecnologie zootecniche

Antonello Ledda

Elisabetta Manca

Cristiano Manni

Rita Marras

Dottore di Ricerca/Ph.D.: **Antonello Ledda**

Data di Discussione della Tesi/Date of Thesis Defense: **1.3.2018**

Titolo della Tesi/Thesis Title: "**Permanent effects of starch and fiber supplied during uterine and postnatal life on first lactation performance of dairy sheep**"

Tutor/Adviser: **Antonello Cannas**; Co-Tutor/Co-Adviser: **Alberto Stanislao Atzori**

### **Abstract**

This Thesis shows the lactation performances of sheep exposed to different dietary carbohydrates during uterine life, growing and mid lactation. The first Chapter is a literature overview of dietary carbohydrates, nutrient partitioning in lactating sheep, physiological mechanisms of insulin resistance and basis of fetal programming. The experimental hypothesis: early exposure to dietary starch or fiber might induce permanent changes of glucose metabolism increasing lactation persistency of first lactating sheep. The second Chapter described the experimental design. The third Chapter presented the lactation performances of primiparous sheep fed different carbohydrates (starch and fiber) in mid lactation. Dietary treatments did not significantly affect sheep performance. The fourth Chapter described effects of starch and fiber supplied during: 1) uterine life, 2) growing and 3) mid lactation on sheep lactation performances. Results showed that sheep exposed to starch early in life, fed fiber diets in mid lactation, had higher lactation persistency. This effect was statistically significant only for a small group of sheep in homogenous physiological status. The fifth Chapter showed results of glucose and insulin tolerance tests performed in pregnancy and lactation. Observed patterns indicated that early in life exposure to starch might induce higher insulin resistance whereas exposure to fiber might induce higher insulin sensitivity. Finally, general conclusions close the dissertation.

Dottore di Ricerca/Ph.D.: **Elisabetta Manca**

Data di Discussione della Tesi/Date of Thesis Defense: **1.3.2018**

Titolo della Tesi/Thesis Title: **"Use of multivariate discriminant methodologies in the analysis of phenotypic and genomic data of cattle"**

Tutor/Adviser: **Corrado Dimauro**

### **Abstract**

The present thesis is organized in 4 main chapters.

The Chapter 1 is the general introduction and it regards the use of the multivariate statistical techniques in animal science, with a particular emphasis on the discriminant analysis.

In Chapter 2, a new statistical method called Discriminant Association Method (DAM) was proposed. The DAM approach, developed by using multivariate statistical techniques, overcomes most of problems that affect the single SNP regression technique used in the ordinary GWAS.

In Chapter 3, a new index to evaluate feed efficiency was defined: the residual concentrate intake (RCI). RCI identifies efficient and inefficient bovines in converting the concentrate. RCI can be quite simply evaluated and, in consequence, it could be easily included in genomic breeding programs. In the present research, the DAM method was applied to develop a GWAS for selecting markers associated to RCI.

The research reported in Chapter 4 was aimed to develop an algorithm able to early identify highly persistent lactations. Four different models were fitted to individual lactations by using the first 90, 120 and 150 days in milking. Two multivariate statistical techniques were exploited: the canonical discriminant analysis (CDA) and the discriminant analysis (DA). The proposed algorithm combines the talent of curve models in depict features of the lactation and the ability of multivariate statistical techniques in distinguishing differences between groups.

Dottore di Ricerca/Ph.D.: **Cristiano Manni**

Data di Discussione della Tesi/Date of Thesis Defense: **1.3.2018**

Titolo della Tesi/Thesis Title: **"Aspetti del paesaggio zootecnico della Sardegna"**

Tutor/Adviser: **Giuseppe Pulina**

### **Abstract**

The landscape of Sardinia is eminently zootechnical. It is a paradigm of the archaic mediterranean pastoral landscape, because the processes that have generated and maintained it through the centuries have been preserved.

First of all, sheep farming, around which culture still spins the life of the island. The zootechnical landscape is defined by an analysis of the most interesting concepts proposed by various authors, and is dealt in analytical terms, trying to map a variable that expresses the probability of incurring a zootechnical landscape, and from a historical and cultural point of view, re-proposing the work of the geographer Le Lannou, for a subdivision of the land into macro-landscapes. Finally, it is evident that the zootechnical landscape evolves, along with changes in the zootechnical sector, towards new configurations that call into question the forest, and therefore forest landscapes.

Dottore di Ricerca/Ph.D.: **Rita Marras**

Data di Discussione della Tesi/Date of Thesis Defense: **25.5.2018**

Titolo della Tesi/Thesis Title: **"Investigation on meteorological variables affecting sheep bulk milk quality in Sardinian farming systems"**

Tutor/Adviser: **Nicolò Pietro Paolo Macciotta**; Co-Tutor/Co-Adviser: **Giustino Gaspa**

### **Abstract**

Milk yield, quality and composition are influenced by several factors. Various studies investigated how heat stress acts on milk production, with special focus on dairy cattle. In Sardinia's economy, sheep farming plays a crucial role but harsh climatic conditions may affect negatively milk quantity and quality. In this study, this effect was assessed on dairy sheep by statistical analysis of bulk milk characteristics at farm level in Sardinia. The main relationships among relevant variables of about 5000 farms were analysed to detect how farm facilities, geographical and meteorological variables affect milk traits. Furthermore, we quantified losses in milk quantity and quality due to heat stress by means of temperature humidity index (THI). A mixed model was used to predict milk characteristics and the effect of heat stress in a low-cost determination. Multivariate statistics on meteorological variables, referred to the whole island in the late spring and summer, produced an alternative index describing the heat stress condition. We do not observed a close relationships between farm structural variables and milk composition traits in Sardinian farms. When  $THI < 68$ , lactose content was higher whereas fat, proteins and caseins percentages are lower. Compared to the average milk production assumed as 100% a drop of 5% of milk every 10 THI point was estimated. Mixed model analyses highlighted a relevant quota of trait variance explained by random flock effect (from 32 to 64%).

**Corso di Dottorato in Scienze Biomediche**

—

**Ph.D. Program in Biomedical Sciences**

Coordinatore/Coordinator: Prof. Andrea Piana

Dottori di Ricerca/Ph.D.

Curriculum Fisiopatologia medica

Sebastiana Maria Atzori

Maria Luisa Biggio

Dottore di Ricerca/Ph.D.: **Sebastiana Maria Atzori**

Data di Discussione della Tesi/Date of Thesis Defense: **20.2.2018**

Titolo della Tesi/Thesis Title: **"Elastografia epatica: metodiche a confronto"**

Tutor/Adviser: **Gianpaolo Vidili**

### **Abstract**

Background: Ultrasound-based non-invasive methods for evaluation of liver disease severity are becoming increasingly used. This study aimed to compare liver stiffness assessed by 3 shear wave elastography techniques: Philips EPIQ7™; Siemens Acuson™ Virtual Touch Tissue Quantification and Transient Elastography (TE) measured by Echosens Fibroscan™. Results of these 3 methods were compared to histological results in patients with chronic liver disease of different aetiologies. Results: 110 consecutive patients with liver disease underwent a same day liver biopsy and liver stiffness assessment. The results were compared with histological results. A direct correlation was observed between LS values assessed by TE elastography by Elast PQ and VTQ ( $p < 0.0001$ ) and Metavir score. Areas under the Curve (AUC) are: TE 0.829; Elast PQ 0.804; VTQ 0.696 for no or mild fibrosis (F0-F1 n=51) and TE 0.946; Elast PQ 0.866; VTQ 0.852 for cirrhosis (F4, n= 15 positives). The mean optimal cut-off for no or mild fibrosis F0-F1 (n=51) are 8.15 kPa for TE (sensitivity (se) 0.76 and specificity (sp) 0.80); 7.15 KPa (se 0.72; sp 0.80) for ElastPQ and 8.2 KPa (se 0.70 and sp 0.60) for VTQ. Conclusions: TE and Elast PQ correlate well with histological scores of liver fibrosis and perform better than VTQ. The optimal cutoff values for the various degrees of fibrosis are different for each scanner.

Dottore di Ricerca/Ph.D.: **Maria Luigia Biggio**

Data di Discussione della Tesi/Date of Thesis Defense: **20.2.2018**

Titolo della Tesi/Thesis Title: **"Danno ossidativo ed aggregati proteici nella Sclerosi Laterale Amiotrofica: possibili target diagnostici e terapeutici"**

Tutor/Adviser: **Roberto Manetti**

### **Abstract**

**Aim:** Riluzole is the only available cure for ALS, with limited effects for patients and diagnosis is based only on exclusion criteria for other diseases. Oxidative stress and misfolded proteins aggregation play a main role in ALS pathogenesis. We would propose Cerium oxide nanoparticles (CeONPs) as pharmacological adjuvant in Riluzole treatment and VAPB protein as new non-invasive targets for an early diagnosis.

**Methods:** PBMC and fibroblasts were isolated from ALS and Parkinson's patients and healthy controls. CeONPs were added in murine hSOD1wt/G93A NSC-34 and human fibroblasts and H<sub>2</sub>O<sub>2</sub> 100 $\mu$ M was used to induce oxidative stress. CeONPs effects on cell survival, mitochondrial activities, oxidative stress and misfolded proteins aggregates were evaluated. Meantime PBMC were used to evaluate aggregates presence and markers of apoptosis and oxidative stress were evaluated.

**Results:** We identified optimal CeONPs concentration that induces a slightly protective effect on oxidative damage in both human fibroblasts and murine cells. As regard VAPB, we identified a high presence of VAPB aggregates in ALS patients respect to healthy controls and a substantial re-organization and re-distribution of ER. Cell VAPBwt/P56S cultures revealed high levels of oxidative stress markers and ubiquitinated proteins.

**Conclusions:** Preliminary results confirm that protein aggregates and oxidative stress could be markers for early and more specific diagnosis for ALS. Moreover, CeONPs treatment could open perspective to its used as pharmacological adjuvant for Riluzole therapy. Further experiments are needed to confirm our data.

Dottori di Ricerca/Ph.D.

Curriculum Medicina di genere, dell'uomo, della donna e del  
bambino

Francesca Cugurullo

Francesco Dessole

Dottore di Ricerca/Ph.D.: **Francesca Cugurullo**

Data di Discussione della Tesi/Date of Thesis Defense: **28.2.2018**

Titolo della Tesi/Thesis Title: **"Follow up prenatale e post natale dei feti IUGR: differenza di genere"**

Tutor/Adviser: **Salvatore Desso**

### **Abstract**

**Aim:** The purpose of this study was to determine if there is a difference in perinatal outcome by gender among growth-restricted fetuses.

**Methods:** This was a retrospective cohort study of intrauterine growth restriction (IUGR) singleton pregnancies over a one year period. Clinical outcomes compared by gender included preterm delivery, perinatal mortality (PNM), respiratory distress syndrome (RDS), grade 3 or 4 intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), and periventricular leukomalacia (PVL). Statistical analysis included bivariate and multivariable techniques.

**Results:** One hundred singleton pregnancies with IUGR were identified in our Clinic. Fortyseven (47.6%) were males. Birth weight was similar between the groups. After adjusting for maternal demographics, medical history, gestational age, mode of delivery, and antenatal corticosteroids, adverse perinatal outcomes were similar between the groups. Severity of outcomes was also similar between males and females.

**Conclusion:** The general concept that male fetuses have a lower clinical performance than females apparently does not apply in the case of intrauterine growth restriction. The scales are tipped by females, who are more prone to develop IUGR.

Dottore di Ricerca/Ph.D.: **Francesco Dessoie**

Data di Discussione della Tesi/Date of Thesis Defense: **28.2.2018**

Titolo della Tesi/Thesis Title: "**Differenze di genere nei neonati figli di madri diabetiche**"

Tutor/Adviser: **Giampiero Capobianco**

### **Abstract**

Aims: to evaluate two populations of women: one consisting of patients with type I diabetes mellitus (DMI) and another from patient with gestational diabetes mellitus (GMD) and the prevalence of maternal-fetal and neonatal outcomes based on gender differences. Methods: Retrospective study of 57 pregnant women with DMI (24 women, 43%) and GDM (33 women, 57%). Inclusion criteria were: single pregnancy, pregestational diagnosis of type I diabetes. We reported the type of insulin and the number of units per day which was self-administered. We reported the duration of pregnancy, any comorbidities and the value of glycated hemoglobin, whenever possible, in the first trimester of pregnancy. Each woman's obstetric history has been collected as nulliparity, multiparity, history of previous abortions, a history of previous fetal deaths and pre-eclampsia. Obstetric maternal-fetal outcomes we analyzed were: pre-eclampsia, elective caesarean section performed or urgency, preterm birth, P-PROM, polyhydramnios, placental abruption, stillbirth and perinatal death and other obstetric complications related to underlying disease. We also considered the percentage of infants admitted to NICU for the appearance of acute respiratory distress syndrome and low Apgar score at 5 minutes after birth.

Results: Although not statistically significant our study has shown that some maternal fetal outcomes such as RDS and IUGR affect predominantly fetal-neonatal male population, especially in the Group of patients with DMI.

Conclusions: We reported gender difference in materno-fetal outcomes in diabetic pregnant women but further studies on larger sample size are needed before drawing definitive conclusions.

Dottori di Ricerca/Ph.D.

Curriculum Neuroscienze

Chiara Fois

Dottore di Ricerca/Ph.D.: **Chiara Fois**

Data di Discussione della Tesi/Date of Thesis Defense: **28.2.2018**

Titolo della Tesi/Thesis Title: **"Peripheral neuromodulation for drug-resistant epilepsy: the effect of short-term transcutaneous trigeminal nerve stimulation on EEG activity"**

Tutor/Adviser: **GianPietro Sechi**; Co-Tutor/Co-Adviser: **Franca Deriu**

### **Abstract**

Aim: Trigeminal nerve stimulation (TNS) has been proven to exert beneficial effects on symptoms of drug-resistant epilepsy (DRE). However, whether and how TNS is able to modulate the electroencephalogram (EEG) background activity in DRE patients is still unknown. We aimed to investigate the effect of acute TNS on EEG activity by conducting qualitative and quantitative analyses on two DRE patient groups, undergoing real or sham TNS. Methods: 22 DRE patients were randomly divided into "sham-TNS" or "real-TNS" group. Real-TNS was delivered bilaterally to the infraorbital nerve with trains of a symmetric biphasic square wave pulse (1-20 mA, 120 Hz), in a cyclic modality for 20 minutes. The sham-TNS protocol mimicked the real-TNS stimulation but at a zero intensity. EEG recordings were collected for each patient 10 minutes pre, 20 minutes during and 10 minutes post TNS delivery. EEG signal was visually analysed for interictal epileptiform discharge (IEDs) and processed by spectral analysis (Fast Fourier Transform). A between and within subject repeated-measures ANOVA was used for statistical analyses. Results: A significant increase of EEG absolute alpha band power was observed in the during real-TNS compared to the sham-TNS ( $F_{2,18}=1.748$ ;  $p=0.006$ ). Conversely, no significant effects were noticed either for quantitative analysis of other frequency bands or for IEDs detection. Conclusion: Short-term TNS is able to induce an acute effect on EEG background composition of DRE patients. In line with recent evidence, alpha rhythm enhancement might be interpreted as an index of functional inhibition, able to influence cortical activity and reduce seizure propensity.

Dottori di Ricerca/Ph.D.

Curriculum Odontostomatologia estetica adesiva e preventiva

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Sanità pubblica

Giulia Abis

Dottore di Ricerca/Ph.D.: **Giulia Abis**

Data di Discussione della Tesi/Date of Thesis Defense: **23.3.2018**

Titolo della Tesi/Thesis Title: "**Diabetes and medical devices: which devices for which patient**"

Tutor/Adviser:**Maria Giuliana Solinas**

### **Abstract**

Diabetes is a chronic disease that occurs when the pancreas does not produce enough insulin. Insulin therapy is a pharmaceutical treatment used to lower blood glucose in all patients with diabetes type 1 (T1D) and type 2 (T2D).

Insulin therapy can be managed by different medical devices technologies such as insulin pumps and insulin pens.

Aim. To draw the profile of patients in insulin therapy with insulin pumps and insulin pens by identifying the variables that influence the choice of two different medical devices.

Tools and Methods. We developed a questionnaire to rate the lifestyles of these patients. Explorative Factor Analysis and Confirmatory Factor Analysis was performed to define and to confirm the factors that describe the profiles of these patients. Regression Models were performed to estimate the effects of observed variables on the choice of medical device and its cost.

Results. General Characteristics, Employment Information and Eating Habit are resulted the factors that define the characteristics of people with T1D and T2D, independently by medical devices used.

Conclusions. The results provide supporting evidence that are useful to the appropriate choice of medical device for insulin treatment. Therefore, next development is to make the results more generalizable in order that they can be used by policy makers in healthcare for a better management of resources and the best appropriateness of the choice of two different medical devices.

Dottori di Ricerca/Ph.D.

Curriculum Oncologia molecolare

Antonella Maria Morette

Dottore di Ricerca/Ph.D.: **Antonella Maria Morette**

Data di Discussione della Tesi/Date of Thesis Defense: **16.2.2018**

Titolo della Tesi/Thesis Title: **"Post-translational regulation of Yap gene, their influence during Hepatocarcinogenesis"**

Tutor/Adviser: **Rosa Maria Pascale**

### **Abstract**

Previous studies showed that Yap1 is over-expressed in hepatocellular carcinoma (HCC). Yap phosphorylation, is the main mechanism to regulating its activation, and role on Hippo pathway. We hypothesized that modulation of Yap1 role in HCC depend on differences in its post-translational modification. We tested this hypothesis by analysing the relationship of post-translational deregulation of Yap1 in different subtypes of HCC, on prognostic bases and differences on genetic predisposition to the disease. F344 and BN rats were housed and treated according to the esistant hepatocyte protocol. Six normal livers, 20 human HCC with better (HCCB) or poorer (HCCP) prognosis, and corresponding surrounding non-tumour livers were used. HepG2, Hep3B and Huh7 cell lines were transfected with pCMV\_empty vectors, pCMV6\_YAP1 or Yap1 siRNA. The samples were used for genes and proteins expression studies, and additional functional experiments. Results: We observed higher expression of Yap1/CTGF axis in dysplastic nodules and HCCchemically-induced in F344 rats, genetically susceptible to HCC. While lesion induced in BN resistant rats, do not show or show lower increase in YAP expression, compared susceptible rats. In human HCCP, levels of YAP1, CTGF, 14-3-3, and TEAD proteins, and YAP1-14-3-3 and YAP1- TEAD complexes were higher than in HCCB. Forced YAP1 over-expression increased cell viability in HepG2, Huh7, Hep3B cells. We observed activation of cell migration and invasivity in Huh7 cells transfected with YAP1 and inhibition of cell migration and invasivity when cells were transfected with YAP1-siRNA. In conclusion, Yap1 post-translational modification favouring its ubiquitination and apoptosis characterize HCC with better prognosis, whereas condition favouring the formation of YAP1-TEAD complexes and cells survival are associated with aggressiveness.

# Corso di Dottorato in Scienze Giuridiche

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## Ph.D. Program in Juridical Sciences

Coordinatore/Coordinator:

Prof. Michele Maria Comenale Pinto

Dottori di Ricerca/Ph.D.

Carlo Attanasio

Carlotta Cherchi

Alessandro Dasara

Nicola Fresu

Marco Monatari

Dottore di Ricerca/Ph.D.: **Carlo Attanasio**

Data di Discussione della Tesi/Date of Thesis Defense: **9.4.2018**

Titolo della Tesi/Thesis Title: "**Obblighi legali a contrarre e attività d'impresa**"

Tutor/Adviser: **Luigi Nonne**

### **Abstract**

In Italian private law, the freedom of contract plays a significant role. This kind of principle makes each person free to choose if conclude or not a contract, to identify contractual partners and also to establish the content of the contractual provisions. However, in some cases the formation of a contract is directly prescribed by law. A typical example of legal obligation to contract could be find in the article 2597 cod. civ., that forces legal monopolist to enter into contracts concerning monopolized goods or services, respecting the principle of equal treatment. The above mentioned provision, in conjunction with article 1679 cod. civ. (which forecasts a similar obligation for the holder of an administrative concession for public transport services), describes a unitary model that maybe could be applied to all legal obligations to contract in the context of business activities.

The present work aims to research if a legal obligation to contract could be derived from the antitrust law, especially from the article 102 TFUE and, regarding to Italian antitrust law, from the article 3, l. n. 287/1990, which prohibits the abuse of dominant position, and also from the article 9, l. n. 192/1998, which forbids the abuse of economic dependence. A related issue concerns the possibility to extend the above mentioned unitary model, established by articles 2597 and 1679 cod. civ., to those which some authors called "new obligations to contract".

Dottore di Ricerca/Ph.D.: **Carlotta Cherchi**

Data di Discussione della Tesi/Date of Thesis Defense: **9.4.2018**

Titolo della Tesi/Thesis Title: "**Carcere e salute: un'indagine sulla sanità penitenziaria tra Sardegna e Lombardia**"

Tutor/Adviser: **Giampaolo Demuro**; Co-Tutor/Co-Adviser: **Alvise Sbraccia**

### **Abstract**

Obiettivo del presente lavoro è quello di ricostruire l'implementazione della disciplina sul passaggio di competenze nella sanità penitenziaria attraverso la percezione che di essa hanno gli operatori sanitari coinvolti nell'erogazione di prestazioni sanitarie in carcere. In tal modo non pretendiamo certo colmare le lacune della ricerca sociologica sul tema. Più semplicemente intendiamo fornire qualche spunto conoscitivo in più, attraverso il filtro di professionisti che si collocano in una via mediana tra l'interno e l'esterno dell'istituzione (Sarzotti 2007). Proprio questa ambivalenza del personale sanitario rende, a nostro avviso, particolarmente interessanti la sua analisi del contesto carcerario e il potenziale innovativo racchiuso nel suo operato. La ricerca ha ad oggetto l'implementazione della riforma sulla sanità penitenziaria, e di conseguenza il livello di tutela della salute garantito, secondo la percezione che di essa hanno gli operatori sanitari. In effetti crediamo che la degradazione del diritto alla salute in carcere (Baccaro 2003), causata dall'afflittività della detenzione e acuita dalla marginalità sociale della popolazione reclusa, imponga al ricercatore di valorizzare costantemente la portata dinamica dello stesso. Preso atto che, a livello sostanziale, il benessere della popolazione detenuta viene garantito in maniera residuale riteniamo necessario concentrarci sulla tutela concreta dello stesso. Crediamo in effetti che, con tutte le criticità insite nell'affrontare questo tema, non si possa perdere di vista il fatto che la salute, seppur compressa, rappresenti il presupposto per l'esplicarsi di un tentativo di umanizzazione della pena (Esposito 2007).

Dottore di Ricerca/Ph.D.: **Alessandro Dasara**

Data di Discussione della Tesi/Date of Thesis Defense: **9.4.2018**

Titolo della Tesi/Thesis Title: **"La continuità territoriale marittima della Sardegna nell'Unione europea"**

Tutor/Adviser: **Michele Maria Comenale Pinto**

### **Abstract**

This thesis assesses the current EU regulatory framework to be followed by Member States when imposing and financing public service obligations in maritime cabotage to, from and between islands. The liberalisation of maritime transport services (Regulation (EEC) N. 3577/1992) has allowed EU countries to impose public service obligations or conclude public service contracts in order to maintain adequate island cabotage. Compensations for the costs of providing public service must comply with EU State aid rules as interpreted by the Court of Justice (The Altmark criteria) and by the Commission in its package of rules on services of general economic interest (The Almunia package). Drawing on examples from Spain, the United Kingdom (Scotland) and France, the research addresses the issue of providing regular maritime transport services between mainland Italy and Sardinia. The privatisation of the former State-owned maritime holding Tirrenia and its subsidiary undertakings was not accompanied by a comprehensive national regulation, leaving room for uncertainty and triggering a formal investigation procedure by the Commission. Meanwhile, public support granted by the Region of Sardinia to the maritime company Saremar was found incompatible with EU State aid rules. Taking account of the most recent legislative proposals, the study discusses the major questions to be dealt with to achieve an effective maritime territorial continuity.

Dottore di Ricerca/Ph.D.: **Nicola Fresu**

Data di Discussione della Tesi/Date of Thesis Defense: **9.4.2018**

Titolo della Tesi/Thesis Title: **"L'analisi della tutela giuridica dei rapporti familiari della persona detenuta nella teoria generale del diritto di famiglia"**

Tutor/Adviser: **Giovanni Maria Uda**; Co-Tutor/Co-Adviser: **Patrizia Patrizi**

### **Abstract**

The concerned research had the aim to deeply examine the current state of the general theory of family law, according to an approach which sees it belonging to the category of social rights, by means of the study of the protection of the main family rights, considered in conjunction with the adult person in custody, and of the way this discipline has been modified over time, due to social changes and thanks to the science of legal psychology.

This paper highlights the theories which recognize the private law as a legal matter more and more mindful of social relationships and more and more looking after the consequences that different private-law institutes unavoidably produce inside the relationships established among the associates.

The family law is no longer on the border between private and public law, but rather in the social law category, understood as a third genus and as a new shared legal tool between private and public law. The issue of the general theory of family law applied to prison law has been dealt purely with psycho-legal tools.

Indeed, the focal point of this work is precisely the analysis of the relationships which tie all the individuals involved inside the detention context and all different profiles, to protect the same relationships according to the references placed before by the general theory of family law.

Dottore di Ricerca/Ph.D.: **Marco Montanari**

Data di Discussione della Tesi/Date of Thesis Defense: **9.4.2018**

Titolo della Tesi/Thesis Title: **"I Nuovi delitti contro l'ambiente"**

Tutor/Adviser: **Gian Paolo Demuro**

### **Abstract**

Questo lavoro analizza la recente riforma dei delitti ambientali attuata con la Legge 22 maggio 2015, n. 68, la quale ha introdotto nel codice penale italiano alcuni delitti contro l'ambiente, oltre ad aver apportato diverse altre importanti innovazioni.

Dopo aver esaminato il generale contesto normativo antecedente alla L. n. 68/2015, nonché la previsione di obblighi di criminalizzazione imposti dal diritto euro-unitario, l'attenzione si focalizzerà sull'esame dei singoli (ormai codificati) delitti ambientali: inquinamento ambientale ex art. 452-bis c.p., morte o lesioni come conseguenza del delitto di inquinamento ambientale ex art. 452-ter c.p., disastro ambientale ex art. 452-quater c.p., delitti colposi contro l'ambiente ex art. 452-quinquies c.p., traffico e abbandono di materiale ad alta radioattività ex art. 452-sexies c.p., impedimento del controllo ex art. 452-septies c.p., omessa bonifica ex art. 452-terdecies c.p.

Tali nuovi delitti risolvono alcuni problemi in passato determinati dalla mancanza di normativa in materia di protezione dell'ambiente all'interno del codice penale italiano, la quale lacuna costituisce la ragione per cui si era più volte dovuto far ricorso ad altre disposizioni di legge per sanzionare le diverse fattispecie di delitti ambientali.

# Corso di Dottorato in Scienze Veterinarie

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## Ph.D. Program in Veterinary Sciences

Coordinatore/Coordinator:

Prof. Fiammetta Berlinguer

Dottori di Ricerca/Ph.D.

Curriculum Qualità e sicurezza alimentare

Romina Panzalis

Daniele Casti

Virginia De Vito

Dottore di Ricerca/Ph.D.: **Romina Panzalis**

Data di Discussione della Tesi/Date of Thesis Defense: **22.2.2018**

Titolo della Tesi/Thesis Title: **"Rilievi epidemiologici e biomolecolari della toxoplasmosi in Sardegna"**

Tutor/Adviser: **Antonio Scala**; Co-Tutor/Co-Adviser: **Anna Paola Pipia**

### **Abstract**

Toxoplasmosis is a foodborne zoonosis transmitted by *Toxoplasma gondii*, a protozoan belonging to the phylum Apicomplexa of great medical and veterinary importance. Our research, conducted in four experimental phases, aimed to acquire epidemiological and biomolecular data on toxoplasmosis of sheep, pigs and goats reared in Sardinia (Italy).

Briefly, in the 1st phase, ELISA test of sera and meat juice and Nested PCR approaches were used for a rapid and sensitive screening of *T. gondii* infection in a randomized sample of 112 sheep slaughtered for human consumption. The 100% of the investigated animals were found positive at least one of the diagnostic techniques. During the 2nd phase, the immune response of sheep and goats reared together in the same flock was monitored. Seroprevalence significantly high found in sheep suggest a greater susceptibility of this species to infections with *T. gondii* compared to goats. In the 3rd phase, it was evaluated the passage of IgG anti-*T. gondii* from 47 Sarda sheep to their respective lambs soon after birth. Serological analysis performed at different time indicate that passive immunity acquired via the colostrum in the lamb is protective for 3 months.

Finally in the last phase a cross-sectional investigation was carried out on animals raised in 109 pig breedings and slaughtered for human consumption. Antibodies against *T. gondii* were found in the 51.7% of the sera samples, while preliminary data on genotyping showed in pigs of the island the presence of the clonal lineage Type III.

Dottore di Ricerca/Ph.D.: **Daniele Casti**

Data di Discussione della Tesi/Date of Thesis Defense: **22.2.2018**

Titolo della Tesi/Thesis Title: "**Prevenzione della Listeriosi: studio della contaminazione negli alimenti di origine animale e sorveglianza attiva in strutture sanitarie**"

Tutor/Adviser: **Christian Scarano**

### **Abstract**

*Listeria monocytogenes* is the cause of a bacterial disease, mainly of food origin called listeriosis. In addition to the gastrointestinal form, it can evolve into a more invasive form causing meningitis, abortion, septicemia and death. The aim of this work is to develop an active hospital surveillance protocol in order to make the epidemiological monitoring of clinical cases of human listeriosis more efficient in relation to the possible food origin, and to define the main phenotypic and genotypic characteristics of strains human or food origin, circulating in Northern Sardinia. The research activities included the definition of the immune profile of subjects with clinical symptoms and acquisition of food-borne strains by sampling on refrigerated RTE (ready-to-eat) food and screening in some work environments. The results obtained show a widespread contamination, almost always compliant with the legal limits of *Listeria monocytogenes*. However the criticality regarding the possible ingestion of these food items by the aforementioned categories of vulnerable consumers appears to be of considerable importance. The data obtained represents an important tool in the prevention and the study of the spreading of listeriosis and the development of active surveillance programs is essential as an instrument to assess the occurrence of the pathology, as they allow the characterization of the isolated strains and the discovery and study of the different clusters.

Dottore di Ricerca/Ph.D.: **Virginia De Vito**

Data di Discussione della Tesi/Date of Thesis Defense: **22.2.2018**

Titolo della Tesi/Thesis Title: **"Pharmacokinetic studies of "off-label" drugs in food producing animals. Quantification of drug residues in different organic matrices"**

Tutor/Adviser: **Mario Giorgi**

### **Abstract**

Four studies were carried out in the present thesis. In the first study 65 poultry chickens were randomly divided into 4 groups: group A (n = 20) and B (n = 20) received the drug orally (PO), in group C (n = 20) the drug was injected by intravenous (IV) route, whereas group D (n = 5) was the control group. The analysis of plasma samples and residues in organs were performed through the HPLC-FL instrument. The second study was divided into 2 phases where at the same 6 lactating goats were given tulathromycin drug before gestation and during lactation postpartum period. In the first phase of the study, tulathromycin was administered at 2.5 mg/kg b.w. by IV and subcutaneous (SC) routes. In the second phase of the study, the same animals were administered with a single IV dose. The analysis of plasma samples and organs were performed through the HPLC-MS/MS instrument. In the third study, 20 laying hens were divided into 3 groups: group A (n=6), B (n=6) and C (n=8). During the first phase group A and B was administered the drug tapentadol by IV and PO routes at the dose of 1 and 5 mg/kg b.w. respectively. In the second phase of study, group C received the drug by PO at a dose of 5 mg/kg b.w. for 5 consecutive days. The eggs were collected for 30 days from the beginning of the experiment. Plasma, egg yolk and album samples were analysed using the HPLC-FL instrument. In the fourth study, 6 lactating goats were divided into 2 groups: group A (n = 3) and B (n = 3) where meloxicam was administered by IV and intramuscular (IM) routes at a dose of 0.5 mg/kg b.w. Milk samples were taken up to 168 h for quantification of drug residues in the organic matrix. The plasma and milk samples were analysed using the HPLC-DAD instrument.

Dottori di Ricerca/Ph.D.

Curriculum Qualità e sicurezza alimentare

Maria Veronica Di Stefano

Antonella Idda

Elisa Serra

Dottore di Ricerca/Ph.D.: **Maria Veronica Di Stefano**

Data di Discussione della Tesi/Date of Thesis Defense: **20.2.2018**

Titolo della Tesi/Thesis Title: **"IGF-I and its role in dairy animals: investigations on Holstein Friesian cows and Sarda sheep"**

Tutor/Adviser: **Maria Consuelo Mura**

### **Abstract**

The aim of this thesis was to investigate the roles of IGF-I in dairy animals, in order to improve their production considering the importance of the dairy sector. In study 1, 98 primiparous and 234 multiparous Holstein Friesian cows were chosen to measure plasma IGF-I concentration by ELISA and to determine how IGF-I changes during days 0-27 post-partum, based on their parity, calving to conception interval, number of insemination needed to conception and positive or negative pregnancy diagnosis. The mean of IGF-I concentration was higher in primiparous than in multiparous cows but no difference was found with their reproductive activity. Moreover, from the above animals 40 cows were selected to evaluate the expression of candidate immune genes, 1-8 days after calving and its connection with IGF-I concentration and health status. Despite the role that IGF-I has on reproduction and immunity system, any interesting connection was observed in this research. In study 2, 214 multiparous Sarda sheep were selected to detect polymorphisms within the 5'UTR sequence of the *IGF-I gene* and to investigate possible association with milk yield and reproduction traits. A SNP (G855C) and a nucleotide variation (G857A) in linkage disequilibrium were found and the animals that carried the G allele produced a significantly higher milk yield compared to the others. In addition, a visible effect, despite not statistically significant, of the G allele on the shortening of the lambing to conception interval was found. It would be interesting to conduct further analysis comprising a higher number of animals to confirm the real frequency and effect that the found SNP has to confirm the strength of the *IGF-I* as candidate gene in animal performances.

Dottore di Ricerca/Ph.D.: **Antonella Idda**

Data di Discussione della Tesi/Date of Thesis Defense: **20.2.2018**

Titolo della Tesi/Thesis Title: "**Studio sulla crioconservazione: dalle cellule somatiche alle cellule staminali**"

Tutor/Adviser: **Sergio Ledda**

### **Abstract**

The challenging theme of cryopreservation was the focus of this PhD project. Different experimental approaches explored this topic in three ovine cell types of somatic, stem and germinal origin.

Skin fibroblasts were cryopreserved at 5°C/min. Cryomicroscopy analysis allowed to observe dynamics of ice formation and to calculate the probability of intracellular ice formation. Gene expression levels of some markers involved in metabolism, apoptosis and pathways of thermal stress were investigated at 0, 24 and 48 hours after thawing, showing that post-thaw in vitro culture could improve cryopreservation outcome.

The second experiment evaluated stem properties and differentiation capacity of primary isolated Wharton's jelly cells and their ability to keep the original characteristics after cryopreservation. Three freezing methods were compared. According to gene expression and immunohistochemistry analysis, the slow and controlled freezing better retained the original cell characteristics than the other two studied methods.

Final experiment was a pilot study aimed to compare standard sperm freezing with a partial freeze-drying method (PFD). Cell motility and physical events as ice formation and the amount of the unfrozen fraction were evaluated via cryomicroscope and environmental scanning electron microscope. Data showed that PFD was better in preserving motility and ensuring a higher unfrozen fraction, limiting severe damages related to ice growth and mechanical pressure.

Dottore di Ricerca/Ph.D.: **Elisa Serra**

Data di Discussione della Tesi/Date of Thesis Defense: **20.2.2018**

Titolo della Tesi/Thesis Title: "**Indagine sulle modificazioni post-traduzionali della tubulina e caratterizzazione funzionale dell'ovocita di ovino adulto e prepubere maturato in vitro e vitrificato**"

Tutor/Adviser: **Sergio Domenico Gadau**

### **Abstract**

Study on tubulin post-translational modifications and functional characterization of ovine oocytes in vitro matured and vitrified.

In the present thesis morphological, ultrastructural and metabolic conditions of adult and prepubertal IVM and vitrified ovine oocytes were explored, In IVM oocytes, by immunofluorescence, several tubulin post-translational modifications (total, tyrosinated, acetylated and detyrosinated, polyglutamylated and  $\Delta 2$  tubulin) were investigated for the first time. Results revealed a well detectable signal only for total, tyrosinated and acetylated  $\alpha$ -tubulin in both sheep and lamb oocytes. As regard tyrosinated and acetylated tubulin, there were no significant differences in their expression in sheep, while in lamb the acetylated level was predominant in comparison with tyrosinated. The different microtubular pattern between adult and prepubertal oocytes, suggest a possible role of microtubules in the acquisition of oocytes competence.

In vitrified adult and prepubertal oocyte we assessed the ability to recover from vitrification-induced damages after warming. Tyrosinated and acetylated  $\alpha$ -tubulin levels, mitochondrial pattern, ROS levels and developmental competence were investigated. Results revealed that vitrified/warmed sheep oocytes need an extra time to restore damage due the cryopreservation procedures. On the contrary the vitrified/warmed lamb oocytes showed structural damages in spindle and chromatin, with high rates of parthenogenetic activations, displaying a lack of molecular tools useful for both cytoskeleton reorganization and developmental competence.

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