Università degli Studi di Torino

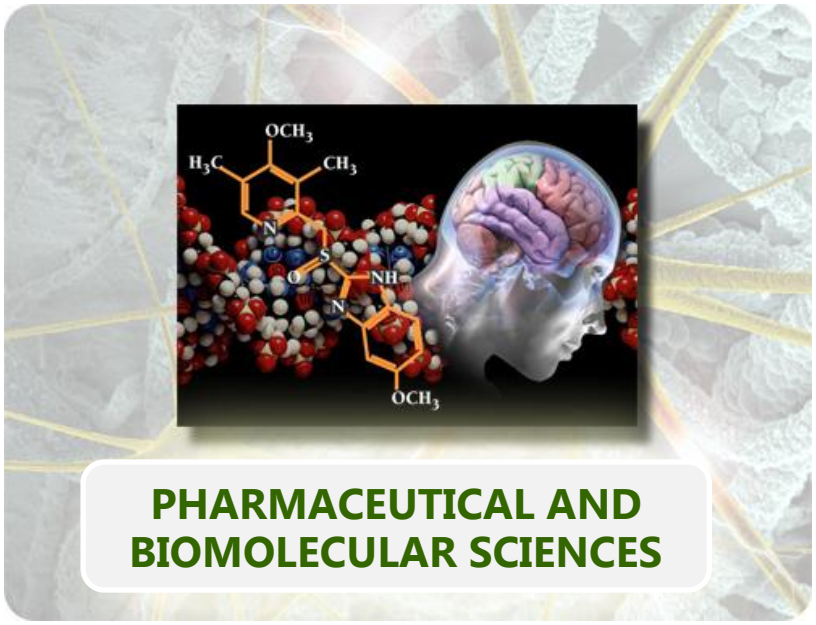
Scuola di Dottorato in Scienze della Natura e Tecnologie Innovative

Dottorato in Scienze Farmaceutiche e Biomolecolari

in collaborazione con

UNIONE INDUSTRIALE TORINO

Advances in



at the University of Torino

Presentazione dei risultati dei progetti di ricerca
dei Dottorandi e delle Dottorande del XXX ciclo

Aula Magna del Rettorato, via Po 17
Venerdì 20 ottobre 2017

Le Dottorande ed i Dottorandi del 30° ciclo del Dottorato in Scienze Farmaceutiche e Biomolecolari si presentano al territorio

Il Dottorato in Scienze Farmaceutiche e Biomolecolari si caratterizza nell'ambito della Scuola di Dottorato di Scienze della Natura e Tecnologie Innovative, cui afferisce, e nell'ambito dell'Ateneo per lo spiccato carattere multidisciplinare, che risulta dal coinvolgimento dei Dipartimenti di Biotecnologie Molecolari e Scienze della Salute, Chimica, Scienza e Tecnologia del Farmaco, Scienze della Sanità Pubblica e Pediatriche, Scienze della Vita e Biologia dei Sistemi. Tale carattere, unitamente a quelli di internazionalità ed intersettorialità, è stato riconosciuto dall'Agenzia Nazionale di Valutazione del Sistema Universitario e della Ricerca (ANVUR) come proprio di una proposta innovativa di formazione alla ricerca. Nelle concretizzazioni operative della intersettorialità (connessione tra sistema universitario e sistema delle imprese) si pone la seconda giornata **"Advances in Pharmaceutical and Biomolecular Sciences @ UniTO"**, appuntamento annuale in cui le **Dottorande ed i Dottorandi giunti al termine del loro percorso formativo di terzo livello presentano i risultati dei loro progetti di ricerca**. Nel 2017 giunge a compimento il **30° ciclo di Dottorato**, e nelle pagine seguenti sono raccolti i riassunti degli **11 progetti di Dottorato** svolti nel relativo triennio. I destinatari non sono solo i componenti della comunità scientifica del Dottorato (nella totalità dei suoi docenti afferenti e dei suoi studenti), ma anche rappresentanti di aziende che operano nell'ambito del territorio regionale, che abbiamo invitato tramite l'Unione Industriale, che ringraziamo per la collaborazione, rappresentanti dei Poli di Innovazione e di Enti di Ricerca.

Il successo della prima edizione dello scorso anno è stato senz'altro dovuto anche alla sede che abbiamo avuto a disposizione per lo svolgimento dell'incontro, l'Aula Magna del Rettorato: per i Dottorandi è significativo sentirsi accolti nel cuore della loro Università. Un sincero ringraziamento va quindi al Magnifico Rettore, per averci concesso l'utilizzo di questo prestigioso spazio anche per questo secondo appuntamento.

Sperando che anche questa seconda edizione sia occasione di contatto e conoscenza reciproca tra attori di primo piano del territorio per la promozione e l'attuazione dell'innovazione ed il Dottorato in Scienze Farmaceutiche e Biomolecolari, sono stati inseriti in questo fascicolo altri elementi di presentazione del Dottorato stesso. Sono quindi elencati i progetti di ricerca delle Dottorande e dei Dottorandi degli cicli attivati successivamente al 30° (ad oggi siamo giunti al 33°), e sono state riportate sintetiche schede informative sulle strutture dove questi giovani svolgono il loro percorso di formazione alla ricerca, e cioè i cinque Dipartimenti (Biotecnologie e Scienze per la Salute, Chimica, Scienza e Tecnologia del Farmaco, Scienze della Sanità Pubblica e Pediatriche, Scienze della Vita e Biologia dei Sistemi) afferenti a questo Dottorato

Concludo, porgendo, a nome di tutta la comunità del nostro Dottorato, un sincero benvenuto a quanti hanno potuto rispondere all'invito a partecipare alla giornata, che ci auguriamo ricca di spunti ed occasioni di interazione.

Il coordinatore del Dottorato
in Scienze Farmaceutiche e Biomolecolari

Prof. Gianmario Martra

SOMMARIO

PROGRAMMA

I riassunti delle relazioni sono disponibili in un'apposita sezione della home page del sito web del Dottorato: http://dott-sfb.campusnet.unito.it

ORARIO	DOTTORANDA/O	PRESENTAZIONE	SETTORE
9.00-9.15		***Apertura dei lavori***	
9.15- 9.45	Bosca Federica	Synthesis, characterization and structure-properties relationship study of molecular and supramolecular systems for sonodynamic therapy applications	Health, (therapeutics)
9.45-10.15	Ferrara Benedetta	Development of new therapeutic approaches based on drug delivery, target therapy and isolation of biomarkers	Health, (therapeutics)
10.15-10.45	Giraudo Alessandro	Development of innovative GABAA receptor ligands using a bioisosteric approach	Health (therapeutics)
10.45-11.00		***coffee break***	
11.00-11.30	Cavallari Eleonora	Novel hyperpolarized probes for the development of metabolic imaging	Health, (diagnostics)
11.30-12.00	Pagoto Amerigo	Novel MRI/Optical imaging agents for targeted diagnosis and treatment of diseases	Health, (diagnostics, surgery)
12.00-12.30	Bressanello Davide	Multidisciplinary approaches in foodomic studies	Food quality
12.30-13.00	Mandrile Luisa	Application of advanced molecular spectroscopies and chemometric analysis to emerging food metrology challenges	Food quality
13.00-14.00		***Pranzo***	
14.00-14.30	Agliassa Chiara	Effects of Earth's magnetic field on plant growth, development and evolution	Agri/Bio
14.30-15.00	Leinardi Riccardo	Interfacial molecular recognition in complex systems: chemical investigation of the interaction between silica surfaces and cell membranes	Health ((nano)-particle safety/toxicology)
15.00-15.30	Trucco Giulia	Oxidative damage in workers exposed to wood dust. The mechanism of action of this carcinogen according to an innovative approach of the molecular epidemiology	Public health
15.30-16.00	Tassinari Roberta	Life and occupational environment, lifestyle and physio-pathological conditions of human populations. An epidemiological study of oxidative stress and health effects to design the best policies of primary prevention	Public health
16.00-16.15		***Chiusura dei lavori***	

Abstract
dei progetti di ricerca
delle Dottorande e dei Dottorandi
del 30° ciclo

(2014-2017)

Synthesis, characterization and structure-properties relationship study of molecular and supramolecular systems for sonodynamic therapy applications

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Tutor: Dr. Alessandro Barge

Sonodynamic therapy (SDT) is an alternative strategy that manages malignancies by the generation of cytotoxic factors after the excitation of sono-sensitive agents (SSA) upon ultrasound irradiation [1]. The detailed mechanisms are still unclear but the SDT pathway is based on photodynamic therapy (PDT) concept. Nowadays PDT has been approved as anticancer treatment for particular cases of tumor (i.e. Photofrin for Barrett's esophagus). The main ingredients in this treatment are: sensitizer molecule (non-toxic drug, first ingredient) able to be excited by light (excitation source, second ingredient) absorption; during the relaxation processes reactive oxygen species (ROS, third ingredient) are generated and these radicals start a series of biological events which cause tumor cells death. The differences between PDT and SDT concern mainly the excitation energy source. SDT exploit the thermal effect induced by acoustic cavitation (obtained by ultrasound or shock-waves) rather than light. Harsh conditions generated by acoustic cavitation, promote important physical changes (including thermal excitation) and chemical reactions. As it has been touched on before, the SDT requires the contemporary presence of cavitation and specific molecules able to be excited and able to generate radicals. Many studies indicate as good candidates for this purpose porphyrins derivative [2].
Hence, this project is aimed to synthesize new sono-sensitive agents (porphyrin backbone) in order to enhance the sonodynamic effect and reducing PDT limitations (skin photosensitivity and low penetration of light into the tissue) after linking them onto specific nanosupport (SWCNT, Graphene, nanoparticles, liposome and nanobubbles). In the case of SWCNT, particular high efficiency has been observed thanks to the intrinsic features of that nano hybrid material. Whereas, the encapsulation of *ad-hoc* designed porphyrin derivatives into nanobubble shell turned out in a new US-activated theranostic agent. Moreover, the activity of new SSAs would be enriched by the addition of targeted moiety with the purpose to drive more selectively the SSA to target cells. The SDT efficacy has been evaluated on HT-29 or LS 174 T cell lines and great proliferation reduction come out. Since the synthetic pathway to obtain porphyrin derivatives is often arduous, natural source of porphyrin derivative (Chlorophyll) has been considered and encapsulated on biocompatible nanosystems. *In vitro* tests to investigate the ability to generate radical species as consequence of ultrasound irradiation are ongoing.

[1] a) Rosenthal I, Sostaric JZ, Riesz P, *Ultrasonic Sonochemistry*., **2004**, 11, 349; b) Tachibana K, Feril Jr L, Ikeda-Dantsuji Y, *Ultrasonics*, **2008**, 48, 253; c) Trendowski M, *Cancer and Metastasis Reviews,* **2014**, 33, 143.
[2] Chen H, Zhou X, Gao Y, Zheng B, Tang F and Huang J, Drug Discovery Today, **2014**, 19(4), 502.

Figure. Schematic representation of sensitizer (S) excitation after US irradiation, and consequent ROS generations with tumor cell death

Development of new therapeutic approaches based on drug delivery, target therapy and isolation of biomarkers

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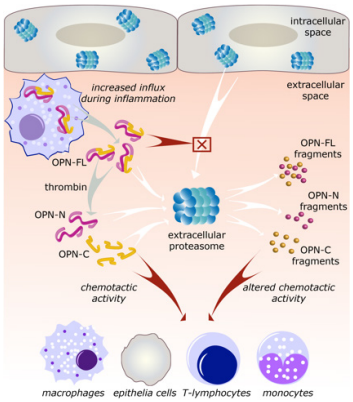
The aim of this project was to investigate new therapeutic strategies in cancer treatment. Chemoresistance, side effects and lack of stability of many drugs, constitute important limits of conventional therapies. In order to overcome them, nano-delivery has been achieving interest as a system able to carry drugs directly to the target tumor site increasing their activity and reducing side effects. In the first part of this work, I focused my study on the evaluation of different nano-formulations. Pyro-βcyclodextrins-nanosponges (βCD-NS) of imiquimod, a potent immunomodulator used in the therapy of topic melanoma, displayed an increased anti-proliferative effect compared to the free drug on several melanoma cell lines. Paclitaxel, another drug commonly used against melanoma that presents limits due to its low stability, delivered by βCD-NS more efficiently inhibited *in vitro* melanoma cell viability, migration and angiogenesis, and *in vivo* tumor growth. Different nano-carriers, such as solid lipid nanoparticles (SLN), delivering temozolomide, showed an improved efficacy against melanoma *in vitro and in vivo*. This study has also been extended to chemoresistant tumor cell lines, using GSH/pH responsive nanosponges delivering strigolactones; they are smart nanocarriers that release drugs "on demand" as a function of intracellular microenviroment. In the second part of this work, I focused the attention on the study of immuno-targets that play an important role in cancer. Osteopontin (OPN), is an inflammatory cytokine cleaved by thrombin during inflammation in two fragments, N- and C-terminal. In tumors, OPN is highly expressed and acts as a proangiogenic factor able to promote metastasis dissemination. OPN is involved in the pathogenesis of multiple sclerosis (MS) and its animal model, experimental autoimmune encephalomyelitis (EAE). For this reason, we evaluated the effects of its two fragments on human cells and EAE by focusing on processes involved in the relapse/remission pattern of MS. The treatment with different OPN forms revealed a coordinated effect of the two OPN fragments on lymphocyte adhesion to human umbilical vein endothelial cells (HUVEC) and migration. Both these processes were supported by OPN-FL, but OPN-C induced only adhesion, whereas OPN-N induced only migration. Another protease that plays a crucial role on OPN activity is 20S proteasome (PR). In MS, plasma extracellular PR levels are increased and mark cell damage and immunological activity. In HUVECs and monocytes, the treatment with 20S PR significantly hampered the chemotactic activity of OPN-N, whereas it increased OPN-FL and especially OPN-C chemotactic activity on HUVEC and lymphocytes. This suggests that PR-mediated degradation of OPN-FL and OPN-C generates novel OPN chemotactic fragments. A mass spectrometry analysis of PR digestion products of OPN-C detected 6 main fragments, which were then synthesized and analyzed. Four of these peptides exerted a strong chemotactic activity towards HUVEC and lymphocytes and two peptides displayed this activity also toward several tumor cell lines, suggesting that they may play a role in tumor metastatic dissemination, since the levels of both OPN and extracellular PR are often high in the tumor mass. Consequent obtained data deriving from the study of OPN role on tumor progression cannot be shown because of patent-protection.



Besides the possibility to find new strategies for cancer treatment, also an improvement in diagnostic methods is needed, in order to prevent disease progression. Therefore, during my period abroad at Universitè Paris Est, I worked on a project with the aim to isolate and study biomarkers that can help in the early diagnosis of pancreatic adenocarcinoma (PDAC), whose very poor prognosis is due to the lack of systems to identify the tumor at early stages. In particular, I carried out a study on PDAC cells released exosomes, which carry molecules responsible of cellular interaction in the tumor microenviroment. A mass spectrometry analysis pointed out that PDAC cells exosomes contained a large number of proteins that showed to be also present in a different amount in PDAC or healthy mice plasma. A qualitative analysis of these proteins revealed a connection between their expression and their role in tumor progression.

Development of innovative $GABA_A$ receptor ligands using a bioisosteric approach

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Tutors: Prof. Marco Lolli; Prof. Bente Frølund

γ-aminobutyric acid (GABA) exerts the main inhibitory function in the central nervous system (CNS) by activating the $GABA_A$ receptors ($GABA_ARs$) and $GABA_B$ receptors. $GABA_ARs$ are ligand-gated ion channels composed by five subunits assembled around the chloride ion conducting pore (Figure 1, left).
Several subunits (e.g. α_{1-6}, β_{1-3}, γ_{1-3}, δ, ρ_{1-3}) assemble together building at least 26 native and mainly heteromeric $GABA_AR$ subtypes.[1] Different regional distribution and functional properties of the individual subtypes suggest involvement in a wide range of functions throughout the CNS.[2] Taking this knowledge, it would be important to disclose the function of each $GABA_AR$ subtypes and investigate the possibility of using orthosteric ligands as therapeutic agents.
The overall aim of this project is the development of new GABA analogues targeting $GABA_ARs$ subtypes. For this purpose, a bioisosteric approach at the carboxylic acid and amino moieties of GABA was evaluated using a diverse series of five membered heterocycles (Figure 1, right).
The synthesis, the pharmacological and physicochemical characterization of novel heterocycles in the $GABA_AR$ area were developed. Dihydroimidazole and 2-amino analogues of dihydrothiazole and dihydroimidazole were chosen and shown to translate into valid novel amino bioisosteres in the $GABA_AR$ area. On the other hand, hydroxy-1,2,5-thiadiazole and 4-hydroxytriazole were developed as carboxylic acid bioisostere for the $GABA_ARs$.
These novel heterocycles were successfully applied as bioisosteres in the $GABA_AR$ area and showed interesting and distinctive pharmacological properties for the $GABA_ARs$.

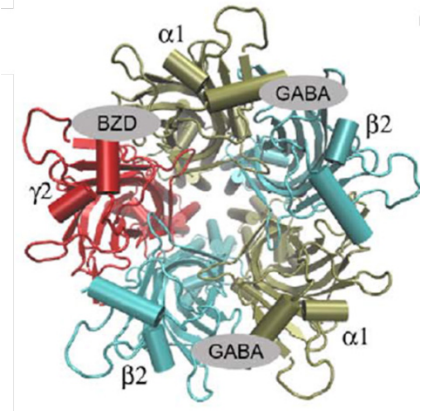

Figure 1. *Left: schematic top view of $GABA_AR$. Right: structures of novel amino and carboxylic acid bioisosteres in the $GABA_AR$ setting.*

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[2] Petersen, J. G.; Bergmann, R.; Krogsgaard-Larsen, P.; Balle, T.; Frolund, B., Probing the Orthosteric Binding Site of GABAA Receptors with Heterocyclic GABA Carboxylic Acid Bioisosteres. Neurochem. Res. **2014**, 39, 1005-1015.

Novel hyperpolarized probes for the development of metabolic imaging

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Tutors: PhD Francesca Reineri

Hyperpolarisation (HP) is a means to overcome the lack of sensitivity of magnetic resonance (MR) and has enabled real-time metabolic imaging (i.e. monitoring metabolic processes *in vivo*, in real time). From the clinical perspective, it can provide valuable diagnostic and prognostic tools. Diagnostics is based on that altered metabolism is usually related to pathological conditions (i.e. the Warburg effect in tumours). Concerning prognosis, the response to the administration of therapies can be detected early, on the basis of the observation of metabolic adjustments.

ParaHydrogen Induced Polarization is an affordable, easy to implement method that may allow wider application of MR hyperpolarized agents than the expensive and technically demanding gold-standard hyperpolarization tool named dissolution-Dynamic Nuclear Polarization (d-DNP). The introduction of PHIP-SAH (PHIP by means of Side Arm Hydrogenation) allowed to considerably extend the applicability of parahydrogen to hyperpolarization of metabolites (pyruvate and lactate) that seemed unobtainable, before, using this hyperpolarization source.

This process relies on the following steps: 1) functionalization of the acid with an unsaturated alcohol (side-arm), 2) addition of parahydrogen to the side arm, 3) polarization transfer from parahydrogen to the target ^{13}C carboxylate signal, 4) side arm removal (hydrolysis of the ester). In this context, ^{13}C-HP pyruvate is the most studied metabolite (e.g. pyruvate conversion in lactate can be monitored).

My PhD work shows the applications of these substrates for metabolic studies *in vitro* (on breast cancer cells) and *in vivo* (healthy mice, cardiac dysfunction model and breast cancer model). The team I belongs carried out leading-edge experiments during the last years in the field of PHIP-SAH for the hyperpolarization of pyruvate and lactate. We obtained hyperpolarized injectable solutions of pyruvate and lactate with polarization in the range of 4-7% that have been used for metabolic studies both *in vitro* and *in vivo*. The production method is fast, starts from stocked reagents and has been optimized to be as simple as possible with the potential to be translated to an automatic production process.

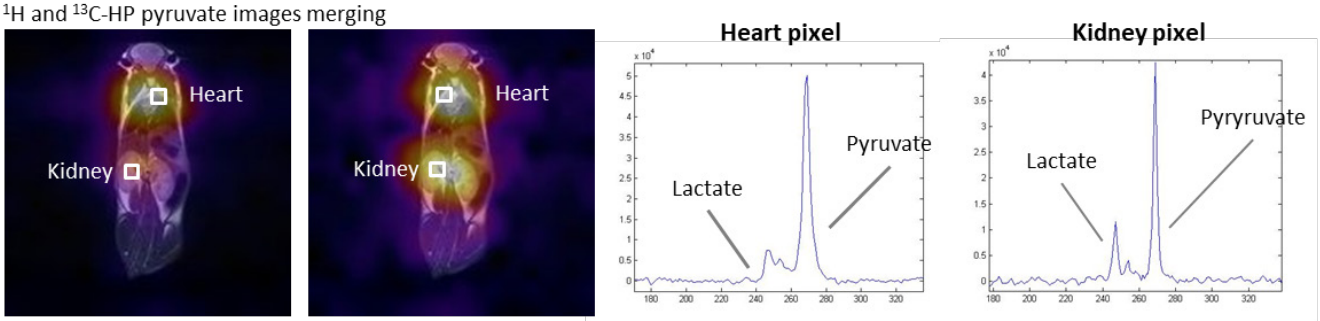
During these three years, it has been demonstrated that the biocompatible aqueous solution of HP-pyruvate and HP-lactate obtained by the PHIP-SAH method provide information about the rate of metabolic conversion that are consistent with results obtained with other conventional methods.

My PhD work was the first metabolic imaging study of cancer carried out using ^{13}C hyperpolarized pyruvate obtained through the cost effective and easy to handle PHIP-SAH method.

Today, preclinical development of PHIP-SAH is ongoing, but, despite solid preclinical results are still needed to guide and stimulate its clinical translation, a translation of PHIP-SAH into a standard preclinical research tool and even to clinical trials can be easily foreseen.

In conclusion, the introduction of PHIP-SAH methods in the clinical use will provide clinicians with better diagnosis and prognosis leading to more personalized and effective patient treatments.

^{1}H and ^{13}C-HP pyruvate images merging



^{1}H and ^{13}C-HP lactate images merging

Novel MRI/Optical imaging agents for targeted diagnosis and treatment of diseases

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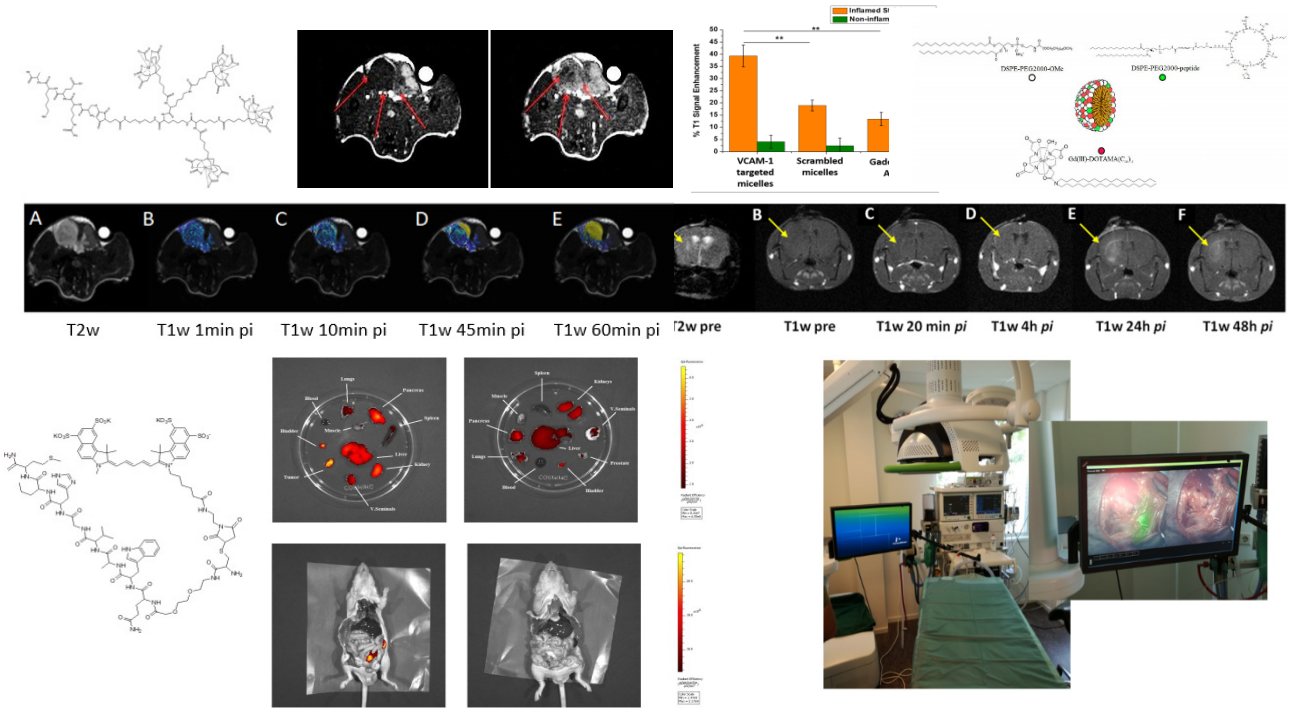
Targeted molecular imaging offers the possibility to widely improve the quality of diagnosis and treatment for different pathological conditions. My PhD project has been mainly focused into the design, development and test of novel molecular probes for MRI targeted diagnosis and Optical imaging intraoperative applications. Despite the superb spatial resolution of MRI, the lack of sensitivity still remains one of the main drawbacks of this technique in molecular imaging. The use of highly efficient contrast agents conceived to specifically reach the target, it is an established way to overcome this obstacle. For these reasons, two targeted peptide-based probes were synthesized and tested *in vivo* on tumor and inflammation mouse models. The former is the molecular tetramer CREKA-dL-(AAZTA-Gd^{3+})$_4$ that, using the innovative Gd-AAZTA ligand and the small peptide vector CREKA, can interact with the tumor extracellular microenvironment and give a localized *in vivo* contrast on MRI images of prostate cancer. The latter is a micellar nanosystems bearing anti-VCAM-1 peptide, a powerful tool to visualize both peripherical that brain inflammation. As mentioned above, the molecular imaging turned out to be an interesting and useful instrument in tumor treatment. In particular, Imaging Guided Surgery (IGS) is an emerging field that exploits the properties of optical fluorescent dyes to precisely localize the malignant tissue, thus allowing surgeons to remove the tumor mass with the minimum impact on healthy tissues. The near infrared fluorescent dye BBN-Cy5.5 is a peptide-based probe, designed and tested *in vivo* on a mouse model of prostate cancer, where it showed a high potential for real-time intraoperative intervention. Finally, considering the high translational applications of this method, I spent the last part of my PhD in Rotterdam (The Netherlands), deepening the potential of novel molecular dyes on spontaneously developed dog tumors.



Multidisciplinary approaches in foodomic studies

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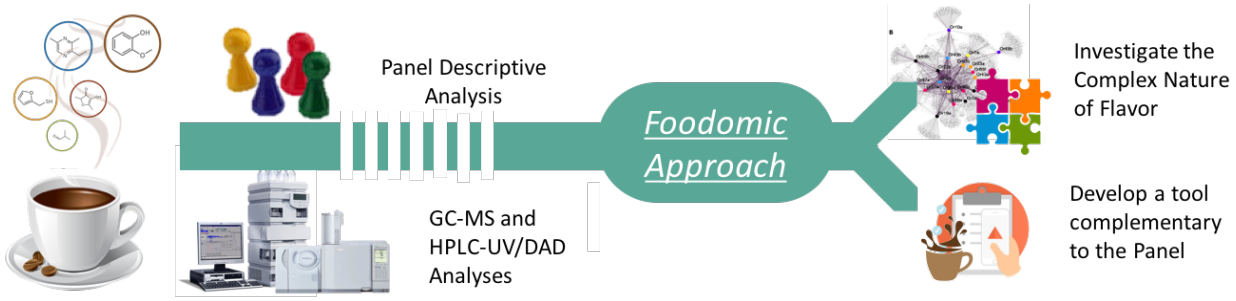
Between the "-omics" disciplines "*Foodomics*"[1,2] is the analytical approach that, in food chemistry, aims to an even more global characterization of the food to define its chemical, physical, sensory and nutritional properties in order to meet always more aware and demanding customers.
A particular brunch of foodomic, focused on linking the chemical composition to the sensory properties of food, assumes particular relevance in the case of recreational foods (like coffee), which choice and consumption is driven more by the pleasure given its intake than by its nutritional properties.
This study aims to investigate the relationship between the chemical composition of coffee flavor and its sensory impact.
This ambitious task has been faced by a multistep project:

- in the first step different analytical platforms and sampling strategies have been used to simulate the panel experience during sensory descriptive analyses[3] (HS-SPME-GC-MS, di-SPME-GC-MS and SBSE-GC-MS to simulate aroma perception and the HPLC-UV/DAD to simulate the tasting experience) and better understand how aroma and taste contribute to the flavor definition.
  the second step involved the definition of the chemical fingerprint of six different sensory notes coupling an informative (but also suitable for routine analyses) platform (HS-SPME-GC-MS) to a chemometric data elaboration.
- a molecular sensory science approach has been used to chemically characterize the *Woody* sensory note on the same coffee samples and obtain an inter-approach validation for the developed "Sensometric" approach.
- a large part of the project has been focused on the data elaboration archived by chemometric tools like PCA, MFA, PLS-DA, parametric and non-parametric regressions to model a prediction tool able to define the coffee quality in cup.

Chemometric models and the *–omic* approach represent a step forward the conventional food flavor analysis because allow a better and more comprehensive investigation of the complex pool of interactions behind the food flavor and moreover, even if the panel's contribution cannot be replaced by the chemical analysis[4], they can be a valid support for quality control purposes.



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Application of advanced molecular spectroscopies and chemometric analysis to emerging food metrology challenges

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The background in which this doctoral study is located is the emerging field of food metrology. This project started in conjunction with the birth of the Food Metrology Program within the Metrology for the Quality of Life Division at the Italian National Institute of Metrological Research (INRiM). The main goal of this thesis is the assessment of advanced vibrational spectroscopies and chemometrics in food metrology framework. Vibrational spectroscopies, in general, represent valuable candidate methods for food analysis because they are known to be sensitive and selective molecular fingerprint technologies which enable rapid, simple and non-destructive analytical determinations (1). The challenge is to reach the best compromise between smart screening methods, suitable for routine application, and the rigorous metrology requirements. If, from one side, the development of rapid and simple methods for *in-situ* analysis is the priority, on the other side, there is the outstanding need of reproducible and non-method-dependent measurement results. The lack of robustness and wide range validation typical of just born analytical methods can be overcome following the metrology principles of traceability to the SI units, calibration, validation and measurement uncertainty (2). Hyperspectral imaging is the mainly explored technique in this thesis, ranging from near infrared spectroscopy to Raman and Surface Enhanced Raman Scattering Spectroscopy (SERS). Chemometric methods were widely used as powerful tools to extract useful information from a big amount of analytical data and to produce valid models for the classification of food samples and the quantification of food contaminants (3). Different topics were studied to attest the versatility and wide range application of the mentioned techniques. First, spectral imaging was coupled with discriminant analysis to set-up a detection method for animal origin components in feed samples (4); second, SERS strategies for the detection of pesticides traces directly on fruits' peel were developed and tested (5), for example a flexible semi-transparent SERS tape was developed (Fig.1); last, chemometric explorative and classification methods were exploited to investigate the influence of geographical origin on the chemical composition of cocoa shells powder. In conclusion this thesis is devoted to investigate some emerging analytical strategies to face the food safety, food security and food provenience issues.

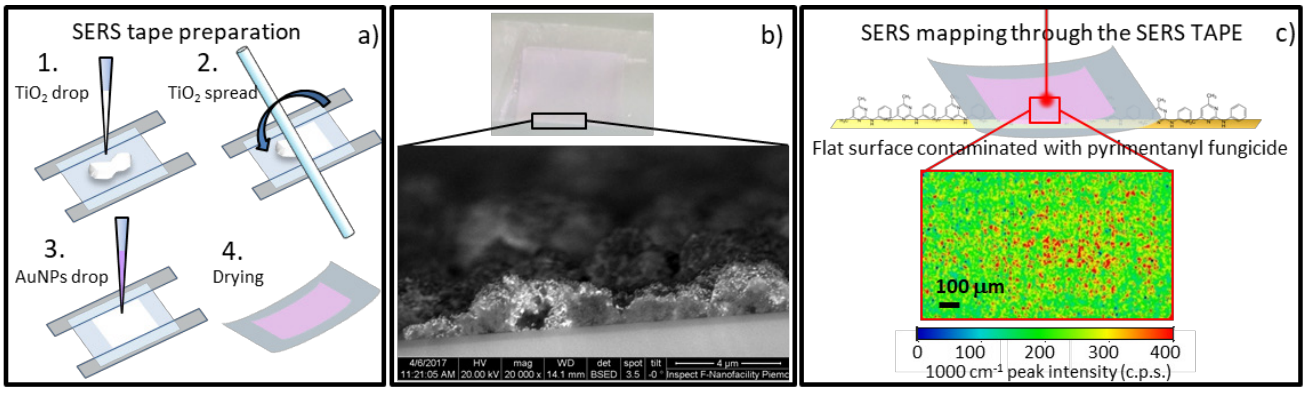

Figure 1:a) preparation steps of a flexible SERS tape: porous layer of TiO_2 and gold nanoparticles are deposited on a sticky scotch tape; b) SEM images of the cross section of the tape; c) SERS mapping through the tape laid on a surface contaminated with pyrimethanil fungicide.

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Effects of Earth's magnetic field on plant growth, development and evolution

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The Earth's magnetic field or the geomagnetic field (GMF) is an environmental factor characterized by local differences in its magnitude and direction at the Earth's surface as well as polarity changes during the so called GMF reversals. Due to its transient instability, GMF is known to influence many biological processes of organisms living on our planet, including plants [1]. Recently, a correlation has been found between the occurrence of GMF reversals and the speciation of Angiosperms, implying a role of GMF in plant evolution [2]. However, the influence of MF of different intensities on plants shows conflicting experimental results and that of a MF lower than GMF has been rarely studied [1]. In particular, the condition of MF absence (Near Null Magnetic Field, NNMF) is becoming of wide interest, since interplanetary navigation will introduce not only plants, but also humans and animals to environments where the natural MF is almost zero. This condition is even the most suitable to investigate in detail the still unclear MF perception mechanism. Up to now, cryptochrome, a blue light photoreceptor, has been suggested as the possible *Arabidopsis* magnetoreceptor, since apparently involved in MF perception in avians [3]. Starting from this background, the general objectives of my PhD were: i) to substantiate the correlation between GMF reversals and plant evolution, testing the response of plants to both normal and reversed magnetic field; ii) to investigate the supposed role of photoreceptors in magnetoreception, evaluating NNMF influence on plant growth processes directly dependent from light perception (such as flowering and photomorphogenesis) using even photoreceptor mutants, iii) to estimate NNMF-induced changes on photoreceptor activation level. As a robust method to generate a stable reverse or reduce MF over a sufficient volume to grow plants, we used a Helmholtz coil system that is not commercially available due to the innovative octagonal shape of its coils. Each couple of coils is connected to a power supply manually controlled by a computer to compensate the GMF or to reverse any of the three GMF dimensions. MF values are monitored by a three-axis magnetometer in real time. All our experiments were performed both *in vitro* and *in vivo* on the model plant *Arabidopsis thaliana*, useful to be used for its fast life cycle, its small dimensions and its fully sequenced genome. Morphological, biomolecular (microarray, RNA-seq, qPCR) and proteomic (Western Blot) approaches were used to reach our objectives. Our data show for the first time that reversing the GMF polarity has significant effects on *in vitro* early plant growth, thus confirming is probable affection on plant evolution. Root length and leaf area were both reduced under the reversed MF, in accordance with the altered expression of genes correlated to plant growth and oxidative response [4]. *In vivo* studies showed that even NNMF was able to affect plant morphology, reducing the leaf area index and the stem length during the plant reproductive growth stages and delaying the flowering time. Differently, we could not see any changes in the photomorphogenic morphology of plant early growth stages. However, NNMF affected not only the expression of genes specific of the early stages of flower induction, but also the expression of some genes correlated to the photomorphogenic response. The transcriptomic profile is even modified in *cry1cry2* mutant by NNMF, thus implying that NNMF also interfers with the expression of gene pathways directly downstream of the activation of photoreceptors others than cryptochrome. Our proteomic analyses confirmed a NNMF negative effect on cryptochrome activation under blue light as well as a repression of phytochrome B degradation under red light in a cryptochrome-dependent manner. Last but not least, the presence of a possible light-independent mechanism of magnetoreception in the roots together with changes in the activation of genes related to biotic and biotic stress response in flowering plants suggested an influence of MF on the global plant trascriptome, confirming the presence of a magnetoreceptor. The obtained results highlight the effective influence of MF on plant growth, thus opening new frontiers of research towards other biological processes and organisms, such as animal models and human cancer cell lines. Changes in GMF polarity and intensity acquire an important value at the evolution level, opening new questions about the evolution of living organisms others than plants. Lastly, the exploration of plant responses to NNMF is a key point for the requirements of plant health status in space missions.

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Interfacial molecular recognition in complex systems: chemical investigation of the interaction between silica surfaces and cell membranes

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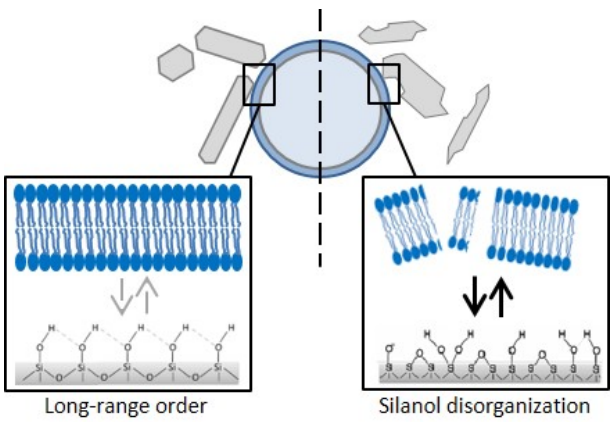
An impressive body of scientific reviews and experimental works,[1-2] has evidenced two key aspects in the interaction between crystalline silica and cells: i) the crucial role played by the particle surface in triggering the adverse biological response, and ii) the extreme variability in the pathogenic potential among different sources of particulate silica.[3] Such a variability is the consequence of differences in silica bulk and surface chemistry, including the occurrence of free radical generation centers ($Si^{\bullet}$ and $SiO^{\bullet}$ as well as redox-reactive metal impurities) and the nature, abundance, and spatial disposition of silanol (–Si-OH) families. Silanols, acidic moieties with a potential for H-bonding, have a key role in defining silica interaction with cells: silica surface is characterized by different families of –Si-OH groups, including isolated (the most common), geminal, and vicinal silanols. The long-range order and distribution of silanol patches on silica surface impart specific characteristics to different silica specimen. Quartz dusts used so far in particle toxicology assays have been obtained by grinding rock containing natural quartz, a process that affects crystallinity and yields samples with extreme variable and complex surface states. To overcome such a variability, we have developed an innovative method to grow highly-pure quartz crystals in respirable size (< 4 µm) with controlled surfaces: such crystals allow us to investigate, at the molecular level, the mechanisms related to quartz toxicity. Surprisingly, the as-grown synthetic quartz crystals with regular faces, characterized by silanol patches with a long-range order, did not show any cellular toxicity on human and murine macrophages, and did not induce rupture/leakage of membrane models (liposome and red blood cells). After inducing the loss of the long-range order of silanol patches by ball milling, synthetic quartz elicited cellular toxicity and strong membranolytic activity. Crystal milling also led to the formation of surface radical species,[4] which are held to be involved in the alteration of the ROS metabolism of cells. Overall, data are consistent with the hypothesis that most of the biological reactivity of quartz dusts is not due to crystallinity *per se,* but it is originated via fragmentation, which entails the formation of conchoidal fractures and new faces. Thus, fracturing upsets the expected long-range spatial order of non-radical surface moieties (silanols, silanolates, siloxanes) and, probably, creates highly-reactive surface silanol patches; accordingly, biological reactivity, and possibly toxicity, appears to be related with the spatial disorganization of surface functionalities.



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Oxidative damage in workers exposed to wood dust. The mechanism of action of this carcinogen according to an innovative approach of the molecular epidemiology

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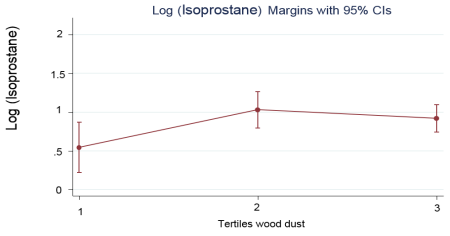
Workplace exposure to wood dust may cause adverse health effects in exposed workers. In 1995 IARC classified hard wood dust as carcinogenic to humans (Group 1). Both hardwood and softwood dusts have a Workplace Exposure Limit (WEL) of 5mg/m^3. Other agents occur in workroom air depend are surface coatings and glues (formaldehyde (FA) and phenol). The traditional epidemiological technique has always been the hallmark approach to demonstrate associations between exposure to hazardous substances and development of disease such as cancer. Therefore, the incorporation of laboratory analytical techniques with traditional epidemiological surveys was integrated in tradition epidemiology to elucidate the biochemical or molecular basis of disease etiology. The aim of the present research is to investigate the role of wood dust occupational exposure in oxidative stress and to contribute to the interpretation about the mechanism involved in diseases-wood dust correlated. Exposure to wood dust is usually associated with exposure to formaldehyde (FA), usually present in every working context concerning the wood; thus, also the FA was measured. Four wood industries were recruited in Piedmont region; three of them produce plywood and one produces doors using soft wood mainly. Personal inhalable dust are collected on a SKC Button Aerosol sampler equipped with PVC fiber filters (Whatman) operating with a flow rate of 4 L/minute (Gilian 5000, Sensidyne, USA). Wood dust concentrations were determined by gravimetric analysis. FA air samples were collected with a radial symmetry sampler (Radiello; Fondazione Salvatore Maugeri, Pavia). Gallic Acid, measured to qualify the dusts, is quantified through liquid chromatography combined with mass spectrometry, UPLC-MS/MS (Acquity UPLC Waters) coupled to a mass detector triple quadrupole (Waters TQD) by Fondazione Salvatore Maugeri, Pavia. Oxidative stress biomarkers were measured in urinary media: 15-F_{2t} IsoP by ELISA technique and 8-oxodG by UPLC-MS/MS (Acquity UPLC Waters). Statistical analysis was carried out with “Stata” (version 12 SE for MS Windows®64 bit). 245 workers were sampled (128 exposed to wood dust, 117 controls). Wood dust, FA have proved to be significantly higher in exposed ($p<0,001$); FA and wood dust are positively correlated among them ($p<0,002$). The analysis of dust shows a significant lower level of contamination in “door industry” and the other industries; this is due to the type of final products and the lower quantity of dust produced by cutting and shaping the wood materials. None industry exceeded the permitted levels by law. The MLR analysis of wood dusts subgrouped in tertiles and adjusted by age and working seniority shows a positive correlation with both the two oxidative stress biomarkers but only by comparing the levels between the first and the second tertile of the dust distribution (0.002 for 15-F2t IsoP and 0.014 8-oxo-dG respectively). The highest exposure levels may result in a form of saturation of the response. The results show that the two selected environmental markers well represent the individual exposures, showing at the same time the different exposure of workers depending on the different occupational context. However, in this study the non-high level of pollution from dust and FA does not seem to induce a significant variation in oxidative stress. The correlation of 8-oxo-dG with wood dusts can be explained with the repair mechanisms of DNA damage; this biomarker is eliminated faster than 15-F_{2t} IsoP[3] probably for different biological mechanism of two biomarkers. However, the preventive action must continue vigorously to reduce as far as possible the risk to workers' health.



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Life and occupational environment, lifestyle and physio-pathological conditions of human populations. An epidemiological study of oxidative stress and health effects to design the best policies of primary prevention

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There is an increasing evidence that bisphenol A (BPA), widely used in the production of plastic products, might be harmful to human health due to its actions as an endocrine-disrupting chemical (EDC) and as inducer of oxidative stress (OS) . Researchers have raised concerns about the use of BPA; this has prompted industry to seek alternative chemicals or to remove BPA from their products; so there has been a gradual shift to using bisphenol analogs, like for example BPS. Bisphenols intake is estimated to be highest in newborns and children because they are thought to be sensitive and fragile to these contaminants. The PhD project deals to investigate the oxidative status in relation with several range of age and with the urinary BPA levels (STUDY 1), and at the same time, to clarify if neonatal exposure to BPA and BPS, during pregnancy and first day of breast-feeding may cause oxidative alterations (STUDY 2).

STUDY 1: 223 urine samples from a population of healthy students (7-19 years old), were analyzed for cotinine as a specific metabolite of nicotine, 15F2t-IsoP as a sensitive biomarker of systemic OS status, and BPA levels. Urinary cotinine was measured by GC/MS; $15F_{2t}$-IsoP was measured with a specific ELISA Kit; finally, BPA-glucuronides were identified by HPLC; while the quantitative analyses were carried out by tandem mass spectrometry with Ion Trap equipped with an Electrospray Ionization Source (ESI). The result of piecewise linear robust regression shows a break point at 1.79 (95%CI: 1.56 - 2.02; $p < 0.001$) of the effect of BPA on 15F2t –IsoP; thus, Isoprostane concentration increases exponentially (more than threefold each one log unit of BPA), when BPA concentration overcomes the break point. MLR analysis shows a positive effect of log-cotinine concentration on log 15F2t-IsoP. In particular, a 12% increment of 15F2t-IsoP is observed for each one-unit-increment of log-cotinine. Furthermore, the result of the relationship between log (ng15F2t - IsoP/mg CREA) and age shows a significant decrease (p=0.026) between infancy (7 - 10 year old) and the beginning of adolescence (11 – 13) and then a new increase after 15 years of age.

STUDY 2: 170 urine and breast milk samples from phisyological and patological (diabetes, hypertension and thyroid disease) mothers hospitalized at the Universitary Unit of Neonatology of the Sant'Anna Hospital, and the corresponding 170 babies' urines were collected for the quantification of 15F2t –IsoP, Cotinine (but only on mother's samples), total (glucoronidate + free) BPA and BPS. $15F_{2t}$-IsoP was quantified by ELISA technique previously described; urinary cotinine was measured by ELISA Kit according to manufacturer's instructions.

Considered that the epidemiological sample is constituted also of newborns with lower concentrations of these contaminants than adults, the identification of urine and breast milk samples were carried out by using UPLC able to detect a very few amounts of bisphenols and equipped with a low-pH resistant reverse phase column. Finally, the quantitative analysis were carried out by tandem mass spectrometry analyzed with a Qtrap equipped with an Electrospray Ionization Source (ESI). At the moment, the setting up of the extraction/quantification method and the analysis are finished, while the statistical analysis are still under processing.

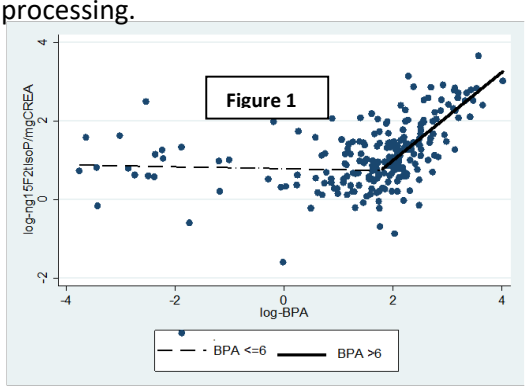
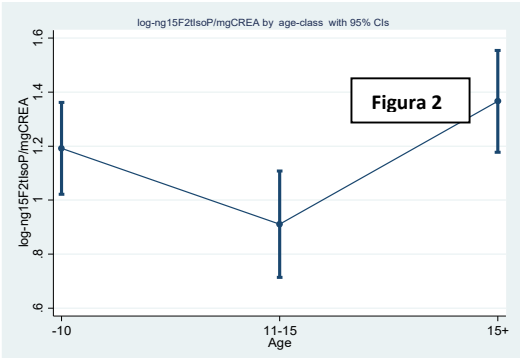


Figure 1. Piecewise linear robust or "hockey stick" regression shows a break point at 1.79 (95%CI: 1.56 - 2.02).

Figure 2. Plot of the relation between log 15F2t –IsoP and age.



Progetti di ricerca con conclusione nel 2018, 2019 e 2020

(cicli 31°, 32° e 33°)

Progetti di ricerca attivi nel triennio 2015-2018
(31° ciclo di Dottorato)

	Nominativi	Progetto	Struttura/e di riferimento*
Dottoranda Tutors	Annasofia Anemone Walter Dastrù (water.dastru@unito.it) Silvio Aime (silvio.aime@unito.it)	Mapping pH in the tumour extracellular region as new MRI biomarker in oncology	Dipartimento di Biotecnologie Molecolari e Scienze per la Salute (DBMSS)
Dottoranda Tutor	Francesca Barbero Cinzia Bertea (cinzia.bertea@unito.it)	Chemical signaling in multitrophic interactions involving plants and insects	Dipartimento di Scienze della Vita e Biologia dei Sistemi (DBIOS)
Dottoranda Tutor	Irene Maria Carnovale Marco Lolli (marco.lolli@unito.it)	Synthesis of new Gadolinium-based contrast agents (GBCAs) for MRI imaging	Dipartimento di Scienza e Tecnologia del Farmaco; progetto finanziato da Bracco Imaging Spa
Dottorando Tutor	Alberto Ciaramella Gianfranco Gilardi (gianfranco.gilardi@unito.it)	Structural and Functional Characterisation of CYP116B5: a new class VII catalytically self-sufficient bacterial P450	Dipartimento di Biotecnologie Molecolari e Scienze per la Salute
Dottoranda Tutor	Alessia Cordaro Enzo Terreno (enzo.terreno@unito.it)	Characterization of fluorescent probes for imaging guided surgery	Dottorato in Apprendistato presso Bracco Imaging Spa; Dipartimento di riferimento: DBMSS
Dottorando Tutor	Gao Chongliang Sheila Sadeghi (sheila.sadeghi@unito.it)	Site-directed mutagenesis studies of human flavin-containing monooxygenase 3	Dipartimento di Scienze della Vita e Biologia dei Sistemi
Dottorando Tutors	Giuseppe Mannino Maffei Massimo (massimo.maffei@unito.it) Andrea Occhipinti (andrea.occhipinti@unito.it)	Chemical analyses and extraction techniques for quality control of food and dietary supplements	Dottorato in Apprendistato presso Biosfered; Dipartimento di riferimento: DBIOS
Dottoranda Tutors	Laura Rotolo Giancarlo Cravotto (giancarlo.cravotto@unito.it)	Enabling technologies for clean and sustainable synthetic processes	Dipartimento di Scienza e Tecnologia del Farmaco
Dottoranda Tutor	Federica Sodano Loretta Lazzarato (loretta.lazzarato@unito.it)	Photoinduced nitric oxide selective release in mitochondria	Dipartimento di Scienza e Tecnologia del Farmaco

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Progetti di ricerca attivi nel triennio 2016-2019
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	Nominativi	Progetto	Struttura/e di riferimento*
Dottorando Tutor	Stefano Acquadro Patrizia Rubiolo (patrizia.rubiolo@unito.it)	Isolation and characterization of plant extracts of pharmaceutical, cosmetic and food interest by bioassay guided studies	Dipartimento di Scienza e Tecnologia del Farmaco
Dottoranda Tutor	Federica Bessone Roberta cavalli (roberta.cavalli@unito.it)	Multifunctional oxygen-filled nanobubbles for the treatment of wound healing	Dipartimento di Scienza e Tecnologia del Farmaco
Dottorando Tutor	Bonanni Davide Marco Lolli (marco.lolli@unito.it)	In silico evaluation of drug design innovative bioisosteric replacement	Dipartimento di Scienza e Tecnologia del Farmaco
Dottoranda Tutor	Cristina Campobenedetto Cinzia Bertea (cinzia.bertea@unito.it)	Chemical characterization of new products with biostimulant action and study of their effects on plant growth and development by using genomic and metabolomic techniques	Dottorato in Apprendistato presso Green Has; Dipartimento di riferimento: DBIOS
Dottorando Tutor	Federico Capuana Silvio Aime (silvio.aime@unito.it)	Design and testing of novel responsive imaging probes	Dipartimento di Biotecnologie Molecolari e Scienze per la Salute; con il supporto del progetto EU-H2020 Single Photon Counting CT
Dottoranda Tutor	Marta Rosso Cialié Chiara Cordero (chiara.cordero@unito.it)	Advanced analytical approaches for “omic” investigations of high quality food matrices of vegetable origin	Dipartimento di Scienza e Tecnologia del Farmaco; progetto finanziato da Ferrero
Dottorando Tutor	Michele Durante Maffei Massimo (massimo.maffei@unito.it)	Sunflower varieties for the food industry	Dipartimento di Scienze della Vita e Biologia dei Sistemi; con il supporto di So.Re.MO
Dottoranda Tutor	Federica Galati Salvatore Adinolfi (salvatore.adinolfi@unito.it)	Characterization of proteins in pathogens as new targets for drug therapy	Dipartimento di Scienza e Tecnologia del Farmaco
Dottoranda Tutor	Ge Xinyu Giancarlo Cravotto (giancarlo.cravotto@unito.it)	Innovative technologies for the recovery, adsorption or degradation of pharmaceuticals and other persistent organic pollutants from industrial or urban waste water	Dipartimento di Scienza e Tecnologia del Farmaco
Dottorando Tutor	Giorgio Grillo Giancarlo Cravotto (giancarlo.cravotto@unito.it)	Design of non-conventional batch and flow chemical processes for biomass valorization	Dipartimento di Scienza e Tecnologia del Farmaco
Dottorando Tutor	Monirul Islam Maffei Massimo (massimo.maffei@unito.it)	Plant magnetoreception: funcional role, molecular biology and physiology of cryptochrome	Dipartimento di Scienze della Vita e Biologia dei Sistemi

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Progetti di ricerca attivi nel triennio 2016-2019
(32° ciclo di Dottorato)

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	Nominativi	Progetto	Struttura/e di riferimento*
Dottoranda Tutor	Francesca La Cava Enzo Terreno (enzo.terreno@unito.it)	Improving the diagnostic efficacy in pathological models with novel high relaxivity gadolinium chelates	Dipartimento di Biotecnologie Molecolari e Scienze per la Salute; progetto finanziato da Bracco Imaging Spa
Dottoranda Tutor	Maria Jesús Morán Plata Katia Martina (katia.martina@unito.it)	Combining ultrasound and microwaves in chemical processes	Dipartimento di Scienza e Tecnologia del Farmaco; dottorato svolto nell'ambito del progetto H2020 COSMIC
Dottorando Tutors	Stefano Nebbia Enrica Pessione (enrica.pessione@unito.it) Laura Cavallarin (laura.cavallarin@ispa.cnr.it)	Effect of food processing on protein structure, functionality and allergenicity	Dipartimento di Scienze della Vita e Biologia dei Sistemi; progetto finanziato da CNR-ISPA
Dottoranda Tutor	Ana Luisa Sotuelo Giancarlo Cravotto (giancarlo.cravotto@unito.it)	Ultrasound- and/or microwave-assisted C=C bond activation	Dipartimento di Scienza e Tecnologia del Farmaco; dottorato svolto nell'ambito del progetto H2020 COSMIC
Dottorando Tutor	Ivano Vigliante Andrea Occhipinti (andrea.occhipinti@unito.it)	Chemical analysis and food processing of sunflower natural extracts	Dipartimento di Scienze della Vita e Biologia dei Sistemi; progetto finanziato da So.Re.MO

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Dottorando Tutor	Simone Cavalera Cristina Giovannoli (cristina.giovannoli@unito.it)	Innovative tests and fast screening methods for self-diagnosis and analyte onsite determinations	Dipartimento di Chimica
Dottoranda Tutor	Debora Collotta Massimo Collino (massimo.collino@unito.it)	Drug targeting of key proximal drivers of the inflammatory unbalance in cardiometabolic diseases	Dipartimento di Scienza e Tecnologia del Farmaco
Dottoranda Tutor	Giulia D'Arrigo Francesca Spyrakis (franscesca.spyrakis@unito.it)	Nuclear receptors: structural and dynamic relationships analysis by innovative in silico methodologies	Dipartimento di Scienza e Tecnologia del Farmaco; Progetto finanziato da Molecular Discovery (UK)
Dottoranda Tutor	Veronika Gunjević Giancarlo Cravotto (giancarlo.cravotto@unito.it)	Enabling technologies in food processing and plant extraction	Dipartimento di Scienza e Tecnologia del Farmaco
Dottorando Tutor	Ivan Hawala Francesca Reineri (francesca.reineri@unito.it)	Synthesis of new AAZTA based bifunctional chelators for the development of innovative PET imaging agents	Dipartimento di Biotecnologie Molecolari e Scienze per la Salute; progetto finanziato da Bracco Imaging Spa
Dottoranda Tutor	Nooshin Nikmaram Silvia Tagliapietra (silvia.tagliapietra@unito.it)	Surface modification of carbon-based nanomaterials for heterogeneous catalysis application	Dipartimento di Scienza e Tecnologia del Farmaco
Dottoranda Tutor	Deyssy Patrucco Silvio Aime (silvio.aime@unito.it)	Synthesis of innovative probes for molecular imaging applications	Dipartimento di Biotecnologie Molecolari e Scienze per la Salute
Dottoranda Tutor	Erica Rebba Gianmario Martra (gianmario.martra@unito.it)	Nanomaterials for the treatment of collagen-based industrial products	Dipartimento di Chimica; progetto finanziato da Kemia Tau srl
Dottorando Tutor	Mirko Sacco Silvio Aime (silvio.aime@unito.it)	Surface functionalization of diamonds for diagnostic applications	Dipartimento di Biotecnologie Molecolari e Scienze per la Salute; progetto finanziato da IIT
Dottoranda Tutor	Rossella Scardaci Enrica Pessione (enrica.pessione@unito.it)	In vitro study on the bacterial responses to human-derived bioactive compounds and feed-back signals.	Dipartimento di Scienze della Vita e Biologia dei Sistemi
Dottoranda Tutor	Giulia Spatola Silvio Aime (silvio.aime@unito.it)	Water in different chemico-physical environments: MRI-MRS characterization and application	Dipartimento di Biotecnologie Molecolari e Scienze per la Salute
Dottoranda Tutor	Giulia Squillacioti Roberto Bono (roberto.bono@unito.it)	Environmental quality, physical characteristics and physical activities in oxidative stress induction in humans having different ages, lifestyles and working conditions.	Dipartimento di Scienze della Sanità Pubblica e Pediatriche
Dottorando Tutor	Federico Stilo Chiara Cordero (chiara.cordero@unito.it)	Italian olive oil sensory quality: advanced analytical strategies for volatile organic compounds chemical fingerprinting	Dipartimento di Scienza e Tecnologia del Farmaco

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(33° ciclo di Dottorato)

(continua)

Dottoranda	Martina Tripepi Silvio Aime (silvio.aime@unito.it)	Design and testing of "smart" probes for multimodal Molecular Imaging applications	Dipartimento di Biotecnologie Molecolari e Scienze per la Salute
Dottorando Tutor	Chao Zhang Gianfranco Gilardi (gianfranco.gilardi@unito.it)	Effect of protein dynamics on the activity of P450 Enzymes	Dipartimento di Scienze della Vita e Biologia dei Sistemi; dottorato nell'ambito dell'accordo UniTO- China Scholarship Council

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FABLAB - Forensic, Analytical & Bioanalytical Laboratories

http://www.chimica.unito.it/do/gruppi.pl/Show?_id=du5p

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SURFIN – Surface and Interface Physical Chemistry

http://www.chimica.unito.it/do/gruppi.pl/Show?_id=cpk9

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DIPARTIMENTO DI SCIENZA E TECNOLOGIA DEL FARMACO

www.dstf.unito.it

Componenti del Collegio dei Docenti (CD) e Tutor (T) del Dottorato afferenti a questo Dipartimento appartengono ai gruppi:

Biochemistry and Molecular Biology (BMB)

http://www.dstf.unito.it/do/gruppi.pl/Show?_id=7tlj

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Medicinal Chemistry -Group MC2

http://www.dstf.unito.it/do/gruppi.pl/Show?_id=8b36

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Medicinal Chemistry - Group NOPhArm (DRUG DESIGN- NO Prodrugs and hybrids)

http://www.dstf.unito.it/do/gruppi.pl/Show?_id=o9ik

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Organic Chemistry

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Pharmaceutical Biology and Food Chemistry

http://www.dstf.unito.it/do/gruppi.pl/Show?_id=82xu

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Prof.ssa Barbara Sgorbini (T)	barbara.sgorbini@unito.it

Advanced Pharmaceutical Nanotechnologies (APN)

http://www.dstf.unito.it/do/gruppi.pl/Show?_id=z3lx

componente del gruppo afferente al Dottorato

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Cardiovascular and Metabolic Pharmacology (CAMP)

http://www.dstf.unito.it/do/gruppi.pl/Show?_id=9l4f

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Cellular Pharmacology (CP)

http://www.dstf.unito.it/do/gruppi.pl/Show?_id=f5dy

componente del gruppo afferente al Dottorato

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Analytical Chemistry

http://www.dstf.unito.it/do/gruppi.pl/Show?_id=kp03

componente del gruppo afferente al Dottorato

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DIPARTIMENTO DI SCIENZE DELLA SANITA' PUBBLICA E PEDIATRICHE

www.dsspp.unito.it

Componenti del Collegio dei Docenti (CD) e Tutor (T) del Dottorato afferenti a questo Dipartimento appartengono al gruppo:

Environmental Hygiene

http://www.dsspp.unito.it/do/gruppi.pl/Show?_id=guh7

componenti del gruppo afferenti al Dottorato

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DIPARTIMENTO DI SCIENZE DELLA VITA E BIOLOGIA DEI SISTEMI

www.dbios.unito.it

Componenti del Collegio dei Docenti (CD) e Tutor (T) del Dottorato afferenti a questo Dipartimento appartengono ai gruppi:

Microbiology and Virology

http://www.dbios.unito.it/do/home.pl/View?doc=research/microbiology_and_virology.html

componente del gruppo afferente al Dottorato

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Plant Physiology

www.plantphysiology.unito.it

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Dr. Andrea Occhipinti (T)	**andrea.occhipinti@unito.it**

Structural and Functional Biochemistry

http://www.biochemistry-scienze.unito.it/Home.html

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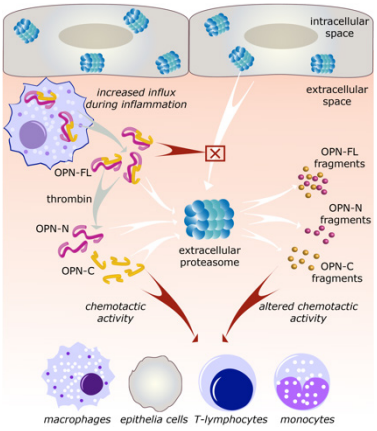
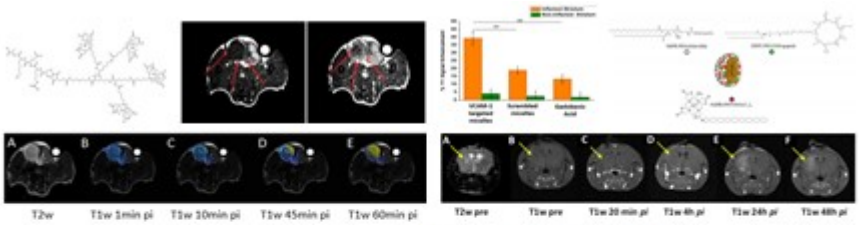
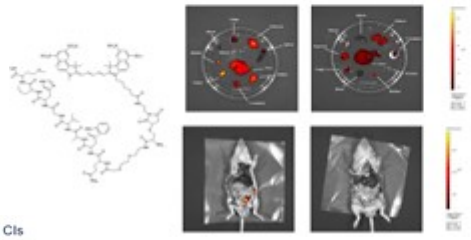
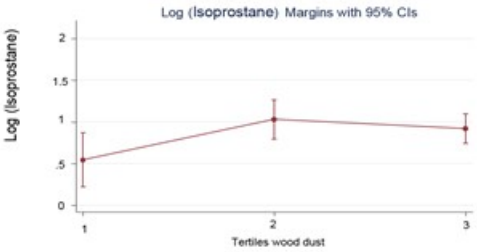
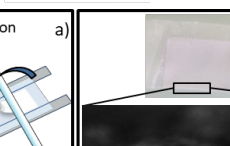
Prof.ssa Enrica Pessione (T)	enrica.pessione@unito.it
Prof.ssa Sheila Sadeghi (CD)	sheila.sadeghi@unito.it
Dott.ssa Francesca Valetti (T)	francesca.valetti@unito.it







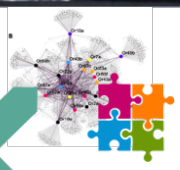




Panel Descriptive Analysis

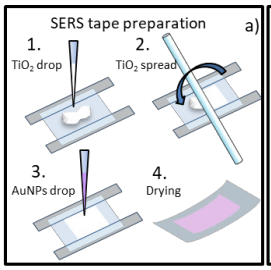
Foodomic Approach

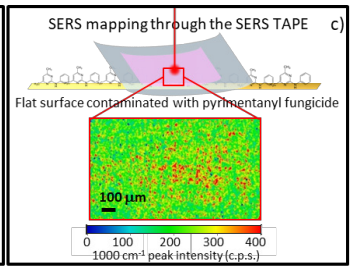
GC-MS and HPLC-UV/DAD Analyses

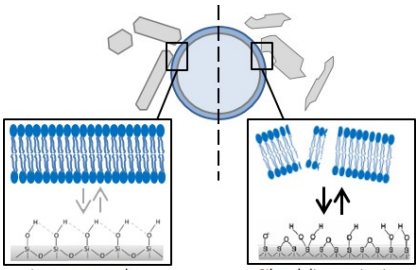


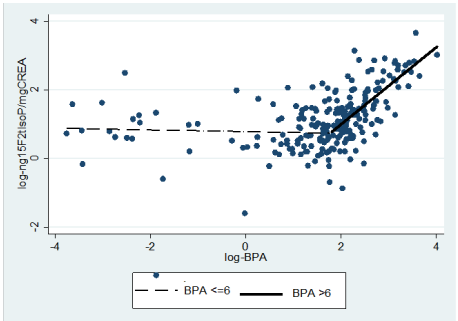
Investigate the Complex Nature of Flavor

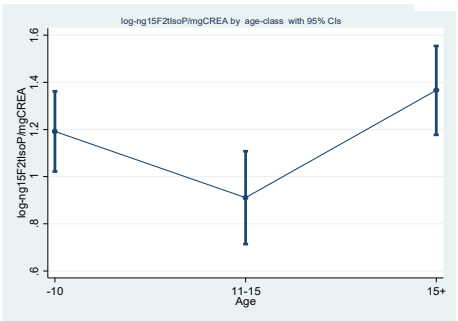
Develop a tool complementary to the Panel

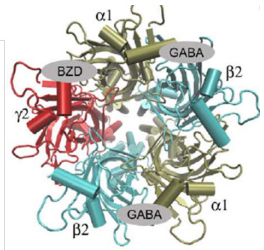




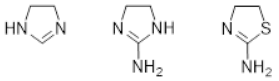




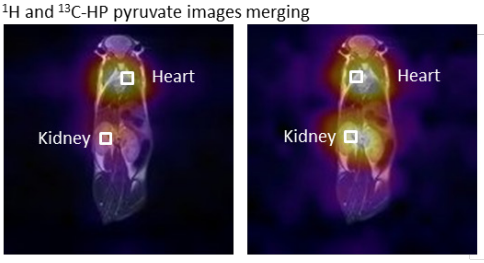


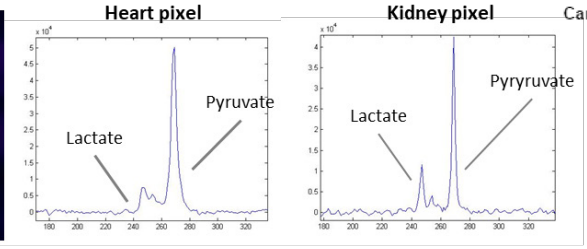


Amino bioisosteres

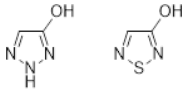


^{1}H and ^{13}C-HP pyruvate images merging





Carboxylic acid bioisosteres



^{1}H and ^{13}C-HP lactate images merging