

# Centro Interdipartimentale di Ricerca per l'innovazione dei Prodotti per la Salute

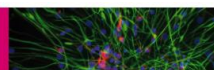
## BIOPHARMANET-TEC



## BIOPHARMANet TEC

### **Allegato 5.1**

### Competenze tecnico scientifiche



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## INTRODUZIONE

Il Centro è articolato in cinque Unità Operative Specialistiche (UO). Ogni UO è coordinata da un Responsabile (RUO) ed è composta da ricercatori e tecnici tra il personale strutturato, e assegnisti e borsisti tra il personale non strutturato.

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Nei seguenti capitoli sono riportate le competenze tecnico-scientifiche specifiche delle singole UO, i brevetti, la partecipazione a progetti nazionali ed internazionali di ricerca finalizzati a partire dal 2013 (o in anni precedenti ma tuttora in corso), e la bibliografia più significativa dal 2013 alla data di stesura di questo manuale. Al termine del documento sono riportate le attività svolte su commessa dalle singole UO finalizzate negli ultimi 2 anni o ancora in essere nel periodo coperto dal presente manuale (Tab. 1).

## 1. UO DRUG DISCOVERY

Questa UO offre competenze di chimica farmaceutica, nei suoi aspetti computazionali (ricerca e progettazione di nuove molecole bioattive, valutazione in silico dei rischi tossicologici), sintetici (messa a punto della sintesi di nuovi composti, produzione di lotti di composti per studi in modelli animali) e bioanalitici (dosamento in fluidi biologici, valutazione di parametri farmacocinetici e degradazioni metaboliche di farmaci).

### Competenze tecnico-scientifiche specifiche

- Inibitori di EGFR ad attività citotossica
- Modulatori del metabolismo degli endocannabinoidi e composti lipidici correlati
- Composti agenti sul sistema melatoninergico
- Composti ad azione antibatterica
- Composti attivi sul sistema nervoso centrale
- Sintesi e modificazione dei carboidrati
- Agenti Anti-miR e Anti-gene
- Chiralità e metodi chiroptici
- Nuovi surfattanti per lo sviluppo di sistemi di gene-delivery e terapia genica.
- Design e sintesi di molecole bioattive per la modulazione dell'espressione genica
- Sintesi di peptidi bioattivi e carrier peptidici
- Studi sull'interazione tra molecole di sintesi e biopolimeri
- Metodi diagnostici e teranostici basati su riconoscimento degli acidi nucleici

### Brevetti

- 22/05/2015. META-SUBSTITUTED BIPHENYL PERIPHERALLY RESTRICTED FAAH INHIBITORS. Piomelli D., Moreno-Sanz G.; Bandiera T; Mor M.; Tarzia G FAAH HK1198644 (A1).
- 13/01/2015 ES2526522 (T3) . 1-(2-FLUOROBIPHENYL-4-YL)-ALKYL CARBOXYLIC ACID DERIVATIVES FOR THE THERAPY OF TRANSTHYRETIN AMYLOIDOSIS. Imbimbo Bruno Pietro; Villetti Gino; Berni Rodolfo. Domana n. ES20110723282T 20110419

### Partecipazione a progetti nazionali di ricerca

- PRIN 2010-11 (20103W4779\_005). Progettazione e sintesi di sonde molecolari per lo studio del ruolo della microglia in patologie correlate alla neuroinfiammazione. Responsabile scientifico dell'Unità di ricerca di Parma: Prof. Gabriele Costantino.

### Partecipazione a progetti internazionali di ricerca

- 2014. INTEGRATE (MSCA-ITN-2014-ETN, H2020). Interdisciplinary Training Network for Validation of Gram-Negative Antibacterial Targets. Grant agreement no: 642620. Università di Parma: Organizzazione di training e networking.

### Bibliografia più significativa

- |   |  |
|---|--|
| <p><b>2015</b><br/>Campanini, Barbara; Pieroni, Marco; Raboni, Samanta; et al Inhibitors of the Sulfur Assimilation Pathway in Bacterial Pathogens as</p> | <p>Enhancers of Antibiotic Therapy. CURRENT MEDICINAL CHEMISTRY Volume: 22 Issue: 2 Pages: 187-213</p> |
|---|--|

Capoferri, Luigi; Lodola, Alessio; Rivara, Silvia; et al. Quantum Mechanics/Molecular Mechanics Modeling of Covalent Addition between EGFR-Cysteine 797 and N-(4-Anilinoquinazolin-6-yl) Acrylamide. JOURNAL OF CHEMICAL INFORMATION AND MODELING Volume: 55 Issue: 3 Pages: 589-599

Scaravaggi, Stefano; Macerata, Elena; Galletta, Michele; et al. Hydrophilic 1,10-phenanthroline derivatives for selective Am(III) stripping into aqueous solutions. JOURNAL OF RADIOANALYTICAL AND NUCLEAR CHEMISTRY Volume: 303 Issue: 3 Pages: 1811-1820

Pieroni, Marco; Annunziato, Giannamaria; Azzali, Elisa; et al. Further insights into the SAR of alpha-substituted cyclopropylamine derivatives as inhibitors of histone demethylase KDM1A. EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY Volume: 92 Pages: 377-386

Gallego-Yerga, Laura; Lomazzi, Michela; Franceschi, Valentina; et al. Cyclodextrin- and calixarene-based polycationic amphiphiles as gene delivery systems: a structure-activity relationship study. ORGANIC & BIOMOLECULAR CHEMISTRY Volume: 13 Issue: 6 Pages: 1708-1723

Dotsey, Emmanuel Y; Jung, Kwang-Mook; Basit, Abdul; et al. Peroxide-Dependent MGL Sulfenylation Regulates 2-AG-Mediated Endocannabinoid Signaling in Brain Neurons. Chemistry & biology Volume: 22 Issue: 5 Pages: 619-28

Curti, Claudio; Sartori, Andrea; Battistini, Lucia; et al. Pushing the Boundaries of Vinylogous Reactivity: Catalytic Enantioselective Mukaiyama Aldol Reactions of Highly Unsaturated 2-Silyloxyindoles. CHEMISTRY-A EUROPEAN JOURNAL Volume: 21 Issue: 17 Pages: 6433-6442

## 2014

Avvakumova, Svetlana; Fezzardi, Paola; Pandolfi, Laura; et al. Gold nanoparticles decorated by clustered multivalent cone-glycolixarenes actively improve the targeting efficiency toward cancer cells. CHEMICAL COMMUNICATIONS Volume: 50 Issue: 75 Pages: 11029-11032

Bernardi, Silvia; Fezzardi, Paola; Rispoli, Gabriele; et al. Clicked and long spaced galactosyl- and lactosylcalix[4]arenes: new multivalent galectin-3 ligands. BEILSTEIN JOURNAL OF ORGANIC CHEMISTRY Volume: 10 Pages: 1672-1680

Berteotti, Anna; Vacondio, Federica; Lodola, Alessio; et al. Predicting the Reactivity of Nitrile-Carrying Compounds with Cysteine: A Combined Computational and Experimental Study. ACS MEDICINAL CHEMISTRY LETTERS Volume: 5 Issue: 5 Pages: 501-505

Capelli, Anna Maria; Costantino, Gabriele. Modelling studies of VEGFR2 and its inhibitors. Conference: 248th National Meeting of the American-Chemical-Society (ACS) Location: San Francisco, CA Date: AUG 10-14, 2014. ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY Volume: 248 Meeting Abstract: 269-COMP

Capelli, Anna Maria; Costantino, Gabriele. Unbinding Pathways of VEGFR2 Inhibitors Revealed by Steered Molecular Dynamics. JOURNAL OF CHEMICAL INFORMATION AND MODELING Volume: 54 Issue: 11 Pages: 3124-3136

Costantino, Gabriele. Computationally driven drug discovery meeting-3-Verona (Italy): 4-6th of March 2014. EXPERT OPINION ON DRUG DISCOVERY Volume: 9 Issue: 12 Pages: 1487-1489

Costantino, Gabriele. Inhibitors of quinolinic acid synthesis: new weapons in the study of neuroinflammatory diseases. FUTURE MEDICINAL CHEMISTRY Volume: 6 Issue: 8 Pages: 841-843

Damiano, Fabio; Silva, Claudia; Gregori, Adolfo; et al. Analysis of illicit dietary supplements sold in the Italian market: identification of a sildenafil thioderivative as adulterant using UPLC-TOF/MS and GC/MS. Science & justice : journal of the Forensic Science Society Volume: 54 Issue: 3 Pages: 228-37

Fiasella, Annalisa; Nuzzi, Andrea; Summa, Maria; et al. 3-Aminoazetididin-2-one Derivatives as N-Acylethanolamine Acid Amidase (NAAA) Inhibitors Suitable for Systemic Administration. CHEMMEDCHEM Volume: 9 Issue: 7 Pages: 1602-1614

Gallego-Yerga, Laura; Lomazzi, Michela; Sansone, Francesco; et al. Glycoligand-targeted core-shell nanospheres with tunable drug release profiles from calixarene-cyclodextrin heterodimers. *CHEMICAL COMMUNICATIONS* Volume: 50 Issue: 56 Pages: 7440-7443

Giannini, Giuseppe; Vesci, Loredana; Battistuzzi, Gianfranco; et al. ST7612AA1, a Thioacetate-omega(gamma-lactam carboxamide) Derivative Selected from a Novel Generation of Oral HDAC Inhibitors. *JOURNAL OF MEDICINAL CHEMISTRY* Volume: 57 Issue: 20 Pages: 8358-8377

Giedroyc-Piasecka, Wiktoria; Dyguda-Kazimierowicz, Edyta; Beker, Wiktor; et al. Physical Nature of Fatty Acid Amide Hydrolase Interactions with Its Inhibitors: Testing a Simple Nonempirical Scoring Model. *JOURNAL OF PHYSICAL CHEMISTRY B* Volume: 118 Issue: 51 Pages: 14727-14736

Gioiello, Antimo; Cerra, Bruno; Zhang, Wujuan; et al. Synthesis of atypical bile acids for use as investigative tools for the genetic defect of 3 beta-hydroxy-Delta(5)-C-27-steroid oxidoreductase deficiency. *JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY* Volume: 144 Pages: 348-360 Part: B

Goh, Ching Yong; Baldini, Laura; Casnati, Alessandro; et al. Upper-rim acidic peptidocalixarenes as crystal growth modifiers. *SUPRAMOLECULAR CHEMISTRY* Volume: 26 Issue: 7-8 Special Issue: SI Pages: 488-499

Lodola, Alessio; Rivara, Silvia; Mor, Marco Insights in the Mechanism of Action and Inhibition of N-Acylethanolamine Acid Amidase by Means of Computational Methods. *BIOMOLECULAR MODELLING AND SIMULATIONS* Book Series: Advances in Protein Chemistry and Structural Biology Volume: 96 Pages: 219-234

Moriconi, Alessio; Cunha, Thiago M.; Souza, Guilherme R.; et al. Targeting the minor pocket of C5aR for the rational design of an oral allosteric inhibitor for inflammatory and neuropathic pain relief. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA* Volume: 111 Issue: 52 Pages: 18799-18799

Pala, Daniele; Castelli, Riccardo; Incerti, Matteo; et al. Combining Ligand- and Structure-Based Approaches for the Discovery of New Inhibitors of the EPHA2-ephrin-A1 Interaction. *JOURNAL OF CHEMICAL INFORMATION AND MODELING* Volume: 54 Issue: 10 Pages: 2621-2626

Pala, Daniele; Scalvini, Laura; Lodola, Alessio; et al. Synthesis and Characterization of New Bivalent Agents as Melatonin- and Histamine H-3-Ligands. *INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES* Volume: 15 Issue: 9 Pages: 16114-16133

Pironi, Marco; Wan, Baojie; Cho, Sanghyun; et al. Design, synthesis and investigation on the structure-activity relationships of N-substituted 2-aminothiazole derivatives as antitubercular agents. *EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY* Volume: 72 Pages: 26-34

Salvio, Riccardo; Cacciapaglia, Roberta; Mandolini, Luigi; et al. Diguandinocalix[4]arenes as effective and selective catalysts of the cleavage of diribonucleoside monophosphates. *RSC ADVANCES* Volume: 4 Issue: 65 Pages: 34412-34416

Spadoni, Gilberto; Bedini, Annalida; Bartolucci, Silvia; et al. Towards the development of 5-HT7 ligands combining serotonin-like and arylpiperazine moieties. *EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY* Volume: 80 Pages: 8-35

Ubertini, Filippo; Laflamme, Simon; Ceylan, Halil; et al. Novel nanocomposite technologies for dynamic monitoring of structures: a comparison between cement-based embeddable and soft elastomeric surface sensors. *SMART MATERIALS AND STRUCTURES* Volume: 23 Issue: 4 Article Number: 045023

### 2013

Artese, Anna; Alcaro, Stefano; Moraca, Federica; et al. State-of-the-art and dissemination of computational tools for drug-design purposes: a survey among Italian academics and industrial institutions. *FUTURE MEDICINAL CHEMISTRY* Volume: 5 Issue: 8 Pages: 907-927

Beato, Claudia; Beccari, Andrea R.; Cavazzoni, Carlo; et al. Use of Experimental Design To Optimize Docking Performance: The Case of

LiGenDock, the Docking Module of Ligen, a New De Novo Design Program. *JOURNAL OF CHEMICAL INFORMATION AND MODELING* Volume: 53 Issue: 6 Pages: 1503-1517

Beccari, Andrea R.; Cavazzoni, Carlo; Beato, Claudia; et al. LiGen: A High Performance Workflow for Chemistry Driven de Novo Design. *JOURNAL OF CHEMICAL INFORMATION AND MODELING* Volume: 53 Issue: 6 Pages: 1518-1527

Bruno, Agostino; Amori, Laura; Costantino, Gabriele Computational Insights into the Mechanism of Inhibition of OASS-A by a Small Molecule Inhibitor. *MOLECULAR INFORMATICS* Volume: 32 Issue: 5-6 Special Issue: SI Pages: 447-457

Capelli, Anna Maria; Bruno, Agostino; Entrena Guadix, Antonio; et al. Unbinding Pathways from the Glucocorticoid Receptor Shed Light on the Reduced Sensitivity of Glucocorticoid Ligands to a Naturally Occurring, Clinically Relevant Mutant Receptor. *JOURNAL OF MEDICINAL CHEMISTRY* Volume: 56 Issue: 17 Pages: 7003-7014

Vacondio, Federica; Carmi, Caterina; Galvani, Elena; et al. Long-lasting inhibition of EGFR autophosphorylation in A549 tumor cells by intracellular accumulation of non-covalent inhibitors. *BIOORGANIC & MEDICINAL CHEMISTRY LETTERS* Volume: 23 Issue: 19 Pages: 5290-5294

Vallerini, Gian Paolo; Arnori, Laura; Beato, Claudia; et al. 2-Aminonicotinic Acid 1-Oxides Are Chemically Stable Inhibitors of Quinolinic Acid Synthesis in the Mammalian Brain: A Step toward New Antiexcitotoxic Agents. *JOURNAL OF MEDICINAL CHEMISTRY* Volume: 56 Issue: 23 Pages: 9482-9495

Pizzirani, Daniela; Pagliuca, Chiara; Realini, Natalia; et al. Discovery of a New Class of Highly Potent Inhibitors of Acid Ceramidase: Synthesis and Structure-Activity Relationship (SAR). *JOURNAL OF MEDICINAL CHEMISTRY* Volume: 56 Issue: 9 Pages: 3518-3530

Ponzano, Stefano; Bertozzi, Fabio; Mengatto, Luisa; et al. Synthesis and Structure-Activity Relationship (SAR) of 2-Methyl-4-oxo-3-oxetanylcarbamic Acid Esters, a Class of Potent N-Acylethanolamine Acid Amidase (NAAA) Inhibitors. *JOURNAL OF MEDICINAL*

*CHEMISTRY* Volume: 56 Issue: 17 Pages: 6917-6934

Radi, Marco; Vallerini, Gian Paolo; Petrelli, Alessia; et al. A one-pot two-step microwave-assisted synthesis of N1-substituted 5,6-ring-fused 2-pyridones. *TETRAHEDRON LETTERS* Volume: 54 Issue: 50 Pages: 6905-6908

Rivara, Silvia; Piersanti, Giovanni; Bartocchini, Francesca; et al. Synthesis of (E)-8-(3-Chlorostyryl)caffeine Analogues Leading to 9-Deazaxanthine Derivatives as Dual A(2A) Antagonists/MAO-B Inhibitors. *JOURNAL OF MEDICINAL CHEMISTRY* Volume: 56 Issue: 3 Pages: 1247-1261

Russo, Simonetta; Incerti, Matteo; Tognolini, Massimiliano; et al. Synthesis and Structure-Activity Relationships of Amino Acid Conjugates of Cholic Acid as Antagonists of the EphA2 Receptor. *MOLECULES* Volume: 18 Issue: 10 Pages: 13043-13060

Sasso, Oscar; Moreno-Sanz, Guillermo; Martucci, Cataldo; et al. Antinociceptive effects of the N-acylethanolamine acid amidase inhibitor ARN077 in rodent pain models. *PAIN* Volume: 154 Issue: 3 Pages: 350-360

Casnati, Alessandro; Sansone, Francesco; Baldini, Laura Special issue of Supramolecular Chemistry honouring Professor Rocco Ungaro PREFACE. *SUPRAMOLECULAR CHEMISTRY* Volume: 25 Issue: 9-11 Special Issue: SI Pages: 535-536

Chudyk, Ewa I.; Dyguda-Kazimierowicz, Edyta; Langner, Karol M.; et al. Nonempirical Energetic Analysis of Reactivity and Covalent Inhibition of Fatty Acid Amide Hydrolase. *JOURNAL OF PHYSICAL CHEMISTRY B* Volume: 117 Issue: 22 Pages: 6656-6666

Pala, Daniele; Beuming, Thijs; Sherman, Woody; et al. Structure-Based Virtual Screening of MT2 Melatonin Receptor: Influence of Template Choice and Structural Refinement. *JOURNAL OF CHEMICAL INFORMATION AND MODELING* Volume: 53 Issue: 4 Pages: 821-835

Moreno-Sanz, Guillermo; Duranti, Andrea; Melzig, Laurin; et al. Synthesis and Structure-Activity Relationship Studies of O-Biphenyl-3-yl Carbamates as Peripherally Restricted Fatty Acid Amide Hydrolase Inhibitors. *JOURNAL OF*



MEDICINAL CHEMISTRY Volume: 56 Issue: 14  
Pages: 5917-5930 Published: JUL 25 2013

Incerti, Matteo; Tognolini, Massimiliano;  
Russo, Simonetta; et al. Amino Acid Conjugates of  
Lithocholic Acid As Antagonists of the EphA2  
Receptor. JOURNAL OF MEDICINAL CHEMISTRY  
Volume: 56 Issue: 7 Pages: 2936-2947  
Published: APR 11 2013

Lodola, Alessio; Capoferri, Luigi; Rivara, Silvia;  
et al. Quantum Mechanics/Molecular Mechanics  
Modeling of Fatty Acid Amide Hydrolase  
Reactivation Distinguishes Substrate from  
Irreversible Covalent Inhibitors. JOURNAL OF  
MEDICINAL CHEMISTRY Volume: 56 Issue: 6  
Pages: 2500-2512 Published: MAR 28 2013

Galvani, Elena; Giovannetti, Elisa; Saccani,  
Francesca; et al. Molecular Mechanisms  
Underlying the Antitumor Activity of 3-  
Aminopropanamide Irreversible Inhibitors of  
the Epidermal Growth Factor Receptor in Non-  
Small Cell Lung Cancer. NEOPLASIA Volume: 15  
Issue: 1 Pages: 61-+ Published: JAN 2013

Galvani, Elena; Alfieri, Roberta; Giovannetti,  
Elisa; et al. Epidermal Growth Factor Receptor  
Tyrosine Kinase Inhibitors: Current Status and  
Future Perspectives in the Development of Novel  
Irreversible Inhibitors for the Treatment of  
Mutant Non-small Cell Lung Cancer. CURRENT

PHARMACEUTICAL DESIGN Volume: 19 Issue: 5  
Pages: 818-832

Galletta, Michele; Scaravaggi, Stefano;  
Macerata, Elena; et al. 2,9-Dicarbonyl-1,10-  
phenanthroline derivatives with an  
unprecedented Am(III)/Eu(III) selectivity under  
highly acidic conditions DALTON  
TRANSACTIONS Volume: 42 Issue: 48 Pages:  
16930-16938

Fu, Jin; Bottegoni, Giovanni; Sasso, Oscar; et al  
A catalytically silent FAAH-1 variant drives  
anandamide transport in neurons (vol 15, pg 64,  
2012). NATURE NEUROSCIENCE Volume: 16  
Issue: 12 Pages: 1907-1907

Costantino, Gabriele; Stilz, Uli. Future priorities  
for EFMC: Interview with Uli Stilz.  
MEDCHEMCOMM Volume: 4 Issue: 5 Pages: 76-  
78

Costantino, Gabriele; Mor, Marco; Pecchini,  
Chiara; et al. Further Insights in 5-phenyl-2-[2-  
(1-piperidinylcarbonyl) Phenyl]-2,3-dihydro-  
1H-pyrrolo[1,2-c]imidazol-1-ones, a Recently  
Disclosed Class of Neuropeptide S Antagonists.  
LETTERS IN DRUG DESIGN & DISCOVERY  
Volume: 10 Issue: 5 Pages: 396-401

## 2. UO DRUG DELIVERY E TECNOLOGIE DI PROCESSO

L'UO si occupa di realizzare, in un contesto regolato da buone pratiche di laboratorio, progetti di ricerca industriale e precompetitiva nell'ambito del drug delivery. Le attività riguardano gli aspetti legati alla formulazione, allo sviluppo industriale e alla fabbricazione di forme farmaceutiche per applicazione orale, transdermica, oculare, nasale e polmonare, nonché la loro valutazione in-vitro. dei medicinali.

### Competenze tecnico-scientifiche specifiche

- Somministrazione di farmaci transdermica, buccale, oculare (uso umano e veterinario)
- Preparazione di forme farmaceutiche solide e semisolide e loro valutazione in termini di proprietà meccaniche e di bioadesione, rilascio e permeazione attraverso barriere biologiche, accumulo nei tessuti.
- Tecniche di enhancement fisico e chimico per aumentare il trasporto di farmaci.
- Applicazioni farmaceutiche dei fluidi supercritici
- Chimica dello stato solido dei materiali per uso farmaceutico
- Polimeri naturali per ingegneria tissutale.
- Studio dei meccanismi e dei sistemi per la progettazione e il controllo delle macchine automatiche impiegate nel settore farmaceutico.
- Flusso di granulari

### Brevetti

- 16/06/2014 Composizione per diluitori per la conservazione a lungo termine di materiale seminale animale. Bettini R., Bianchera A., Bresciani C., Parmigiani E. Domanda di brevetto Italiano n. MI2014A001092
- TW201429478 (A) – 2014-08-01 Mucoadhesive compositions comprising hyaluronic acid and chitosan for topical application. Bettini Ruggero; Bianchera Annalisa; Coruzzi Massimo; Elviri Lisa. Domanda n. TW20130138365 20131024.
- EP2874611 (A1) – 2015-05-27. Gastro-resistant delayed release pharmaceutical form. Colombo Paolo; Rossi Alessandra; Barbieri Stefano; Conti Chiara. Domanda n. EP20130739677 20130718.
- WO2015004519 (A1) – 2015-01-15. New modus of administration of iron, and new formulations adapted for the said goal. Santi Patrizia; Bosi Dario; Lapini Sacchetti Alessandro; Marchi Egidio; Padula Cristina. Domanda n. WO2014IB01303 20140709.
- EP2874610 (A1) – 2015-05-27. Multilayered Pharmaceutical Formulation. Colombo Paolo; Rossi Alessandra; Sonvico Fabio; Barchielli Marco. Domanda n. EP20130739675 20130718.

### Partecipazione a progetti nazionali di ricerca

- 2014-2015 Sviluppo di piattaforme per il delivery polmonare di antibiotici, chemioterapici o antifungini. Responsabile Scientifico: Prof. **Ruggero Bettini**. Ente finanziatore, Regione Emilia Romagna
- 2014-2015. Efficacia dello stanazolo sulla rigenerazione ossea guidata da scaffold biomimetico. Responsabile Scientifico: Prof. **Ruggero Bettini**. Ente finanziatore, Regione

Emilia Romagna.

- Febbraio 2013-Gennaio 2016. PRIN 2010-2011. Studi di frontiera in spettroscopia e dinamica molecolare: da sistemi molecolari semplici ad aggregati supramolecolari e materiali avanzati Coordinatore Scientifico: Prof. Walther Caminati (Università di Bologna). Responsabile Scientifico locale: Prof. **Alberto Girlando**
- 2013-2015. Progetto Telethon TNumber: GGP13036. Trattamento con talidomide del sanguinamento nasale severo ricorrente nella teleangectasia emorragica ereditaria: studio clinico sull'efficacia della somministrazione orale e studio "in vitro" di una nuova formulazione del farmaco per uso locale. Capofila del progetto: Università Di Pavia - IRCCS Fondazione Policlinico San Matteo. Responsabile Scientifico dell'Unità locale: Prof. **Paolo Colombo**.
- 2013-2014. UTS Early Career Research Grant, 10,000 AUD. Prof. **Fabio Sonvico**.
- 2013-2014. CNPq-Brazil Minister of Science, Technology and Innovation, number PVE 401196/2014-3. "Surface-modified nanocapsules for the nasal delivery of poorly soluble drugs: a strategy to treat neurodegenerative diseases" College of Pharmacy at Federal University of Rio Grande do Sul, Brazil. Prof. **Fabio Sonvico**.
- 2013-2014. Azione III - studio delle formulazioni farmaceutiche per gli antivirali selezionati in ragione del virus d'interesse e, conseguentemente, della specie animale e della patologia correlate. Sviluppo di metodi alternativi per la valutazione dell'efficacia di molecole antivirali. Capofila del progetto: Istituto zooprofilattico della Lombardia ed Emilia Romagna. Responsabile Scientifico dell'Unità locale: Prof. **Ruggero Bettini**. Ente finanziatore, Regione Emilia Romagna
- 2013. Progetto SPINNER. Ottimizzazione delle forme molecolari e cristalline di farmaci, fitofarmaci, pesticidi in relazione ad attività, biodisponibilità, aspetti brevettuali, e alla produzione di polimorfi, solvati e co-cristalli con metodi a basso impatto ambientale. Responsabile scientifico: Prof. **Alessia Bacchi**.
- Ottobre 2012-Ottobre 2015. PRIN 2010-2011 "Strategie fisiche per la promozione del trasporto di farmaci attraverso membrane mucosali e attraverso la pelle" Responsabile scientifico dell'Unità di ricerca di Parma: Prof. **Patrizia Santi**. All'interno del programma di Ricerca "Tecnologie avanzate per la veicolazione di molecole farmacologicamente attive attraverso le barriere biologiche dell'organismo".

### **Partecipazione a progetti internazionali di ricerca**

- 10/10/2014. Presentazione della domanda n. 666873-1 per il progetto "COMBINER: Innovative osteogenic combination of bioresorbable chitosan scaffolds and an anabolic drug for the therapy of localized bone defects" nell'ambito della call PHC-16 -2015 "Tools and technologies for advanced therapy" di Horizon 2020. Coordinatore del partenariato: Prof. **Ruggero Bettini**.
- 09/10/2014. Presentazione della domanda n. 666583-1 per il progetto "PINT Novel antimicrobial dry powders inhalers for impromptu treatments" nell'ambito della call PHC-14 - 2015 "New technologies for rare diseases" di Horizon 2020. Coordinatore del partenariato: Prof. **Ruggero Bettini**.

### **Bibliografia più significativa**

**2015**

Bacchi, Alessia; Bourne, Susan; Cantoni, Giulia; et al. Reversible Guest Removal and Selective Guest Exchange with a Covalent Dinuclear Wheel-and-Axle Metallorganic Host Constituted by Half-Sandwich Ru(II) Wheels Connected by a Linear Diphosphine Axle. *CRYSTAL GROWTH & DESIGN* Volume: 15 Issue: 4 Pages: 1876-1888

Bacchi, Alessia; Loffi, Cecilia; Pagano, Paolo; et al. Solid-state and solution characterization of half-sandwich Ru(II) complexes with carboxylic ligands containing N-based coordinating functions. *JOURNAL OF ORGANOMETALLIC CHEMISTRY* Volume: 778 Pages: 1-9

Belotti, Silvia; Rossi, Alessandra; Colombo, Paolo; et al. Spray-dried amikacin sulphate powder for inhalation in cystic fibrosis patients: The role of ethanol in particle formation.. *EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS : OFFICIAL JOURNAL OF ARBEITSGEMEINSCHAFT FÜR PHARMAZEUTISCHE VERFAHRENSTECHNIK* Volume: 93 Pages: 165-72.

Comfort, Claurence; Garrastazu, Gabriela; Pozzoli, Michele; et al. Opportunities and Challenges for the Nasal Administration of Nanoemulsions. *CURRENT TOPICS IN MEDICINAL CHEMISTRY* Volume: 15 Issue: 4 Pages: 356-368

De Robertis, Simona; Bonferoni, Maria Cristina; Elviri, Lisa; et al. Advances in oral controlled drug delivery: the role of drug-polymer and interpolymer non-covalent interactions. *EXPERT OPINION ON DRUG DELIVERY* Volume: 12 Issue: 3 Pages: 441-453.

Martinelli, Francesco; Balducci, Anna Giulia; Rossi, Alessandra; et al. "Pierce and inhale" design in capsule based dry powder inhalers: Effect of capsule piercing and motion on aerodynamic performance of drugs *INTERNATIONAL JOURNAL OF PHARMACEUTICS* Volume: 487 Issue: 1-2 Pages: 197-204

Pescina, Silvia; Govoni, Paolo; Potenza, Arianna; et al. Development of a Convenient ex vivo Model for the Study of the Transcorneal Permeation of Drugs: Histological and Permeability Evaluation. *JOURNAL OF PHARMACEUTICAL SCIENCES* Volume: 104 Issue: 1 Pages: 63-71.

Pescina, Silvia; Sonvico, Fabio; Santi, Patrizia; et al. Therapeutics and Carriers: The Dual Role of Proteins in Nanoparticles for Ocular Delivery. *CURRENT TOPICS IN MEDICINAL CHEMISTRY* Volume: 15 Issue: 4 Pages: 369-385.

Raphael, Anthony P; Garrastazu, Gabriela; Sonvico, Fabio; et al. Formulation design for topical drug and nanoparticle treatment of skin disease. *THERAPEUTIC DELIVERY* Volume: 6 Issue: 2 Pages: 197-216

Rotoli, Bianca M.; Gatti, Rita; Movia, Dania; et al. Identifying contact-mediated, localized toxic effects of MWCNT aggregates on epithelial monolayers: a single-cell monitoring toxicity assay. *NANOTOXICOLOGY* Volume: 9 Issue: 2 Pages: 230-241

Sonvico, Fabio; Coleman, Victoria; Traini, Daniela; et al. Evolved gas analysis during thermal degradation of salbutamol sulphate. *JOURNAL OF THERMAL ANALYSIS AND CALORIMETRY* Volume: 120 Issue: 1 Pages: 789-794

## 2014

Adaila, Kawther; Milenkovic, Milica; Bacchi, Alessia; et al. Synthesis, characterization, DFT calculations, and antimicrobial activity of Pd(II) and Co(III) complexes with the condensation derivative of 2-(diphenylphosphino) benzaldehyde and Girard's T reagent. *JOURNAL OF COORDINATION CHEMISTRY* Volume: 67 Issue: 22 Pages: 3633-3648.

Balducci, Anna Giulia; Cagnani, Stefano; Sonvico, Fabio; et al. Pure insulin highly respirable powders for inhalation. *EUROPEAN JOURNAL OF PHARMACEUTICAL SCIENCES* Volume: 51 Pages: 110-117

Belotti, Silvia; Rossi, Alessandra; Colombo, Paolo; et al. Spray dried amikacin powder for inhalation in cystic fibrosis patients: A quality by design approach for product construction. *INTERNATIONAL JOURNAL OF PHARMACEUTICS* Volume: 471 Issue: 1-2 Pages: 507-515.

Bettini, Ruggero; Bonferoni, Maria Cristina; Colombo, Paolo; et al. Drug Release Kinetics and Front Movement in Matrix Tablets Containing Diltiazem or Metoprolol/lambda-Carrageenan

Complexes. BIOMED RESEARCH  
INTERNATIONAL Article Number: 671532.

Bianchera, Annalisa; Salomi, Enrico; Pezzanera, Matteo; et al. Chitosan Hydrogels for Chondroitin Sulphate Controlled Release: An Analytical Characterization. JOURNAL OF ANALYTICAL METHODS IN CHEMISTRY Article Number: 808703.

Bresciani, Carla; Cabassi, Clotilde S.; Morini, Giorgio; et al. Boar semen bacterial contamination in Italy and antibiotic efficacy in a modified extender. ITALIAN JOURNAL OF ANIMAL SCIENCE Volume: 13 Issue: 1 Article Number: 3082

Brink, Adrian J.; Richards, Guy A.; Colombo, Gaia; et al. Multicomponent antibiotic substances produced by fermentation: Implications for regulatory authorities, critically ill patients and generics. INTERNATIONAL JOURNAL OF ANTIMICROBIAL AGENTS Volume: 43 Issue: 1 Pages: 1-6.

Buttini, Francesca; Miozzi, Michele; Balducci, Anna Giulia; et al. Differences in physical chemistry and dissolution rate of solid particle aerosols from solution pressurised inhalers. INTERNATIONAL JOURNAL OF PHARMACEUTICS Volume: 465 Issue: 1-2 Pages: 42-51.

Carcelli, Mauro; Rogolino, Dominga; Bacchi, Alessia; et al. Metal-Chelating 2-Hydroxyphenyl Amide Pharmacophore for Inhibition of Influenza Virus Endonuclease. MOLECULAR PHARMACEUTICS Volume: 11 Issue: 1 Pages: 304-316

Chierotti, Michele R.; Gobetto, Roberto; Nervi, Carlo; et al. Probing Hydrogen Bond Networks in Half-Sandwich Ru(II) Building Blocks by a Combined H-1 DQ CRAMPS Solid-State NMR, XRPD, and DFT Approach. INORGANIC CHEMISTRY Volume: 53 Issue: 1 Pages: 139-146.

Elviri, Lisa; DeRobertis, Simona; Baldassarre, Stefania; et al. Desorption electrospray ionization high-resolution mass spectrometry for the fast investigation of natural polysaccharide interactions with a model drug in controlled release systems. RAPID COMMUNICATIONS IN MASS SPECTROMETRY Volume: 28 Issue: 13 Pages: 1544-1552.

Girlando, Alberto; Masino, Matteo; Schlueter, John A.; et al. Charge-order fluctuations and superconductivity in two-dimensional organic metals. PHYSICAL REVIEW B Volume: 89 Issue: 17 Article Number: 174503.

INTERNATIONAL JOURNAL OF PHARMACEUTICS Volume: 471 Issue: 1-2 Pages: 507-515

Jeffrey, Reignier M.; Singh, Gurdial; Plaza, Patrice G.; et al. Synthesis of 2,3-O-dibenzylribose and xylosides, and their equilibration studies; Application to oligosaccharide synthesis. ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY Volume: 248

Jeffrey, Reignier; Singh, Gurdial; Plaza-Alexander, Patrice G. J.; et al. Synthesis of 2,3-O-benzyl-ribose and xylose and their equilibration. TETRAHEDRON-ASYMMETRY Volume: 25 Issue: 20-21 Pages: 1424-1429.

Lombardo, Giuseppe M.; Rescifina, Antonio; Chiacchio, Ugo; et al. A top-down approach to crystal engineering of a racemic Delta(2)-isoxazoline. ACTA CRYSTALLOGRAPHICA SECTION B-STRUCTURAL SCIENCE CRYSTAL ENGINEERING AND MATERIALS Volume: 70 Special Issue: SI Pages: 172-180.

Mattarozzi, Monica; Milioli, Marco; Bignardi, Chiara; et al. Investigation of different sample pre-treatment routes for liquid chromatography-tandem mass spectrometry detection of caseins and ovalbumin in fortified red wine. FOOD CONTROL Volume: 38 Pages: 82-87.

Milenkovic, Milica; Cantoni, Giulia; Bacchi, Alessia; et al. Synthesis, characterization and antimicrobial activity of Pd(II) and Fe(III) complexes with ethyl (2E)-2-[2-(diphenylphosphino)benzylidene]hydrazinecarbonylate. POLYHEDRON Volume: 80 Special Issue: SI Pages: 47-52.

Pattarino, Franco; Bettini, Ruggero; Bonda, Andrea Foglio; et al. Polymorphism and kinetic behavior of binary mixtures of triglycerides. INTERNATIONAL JOURNAL OF PHARMACEUTICS Volume: 473 Issue: 1-2 Pages: 87-94.

Pozzoli, Michele; Sonvico, Fabio; Smith, Tim; et al. Evaluation Of Particle Size Distribution Of A Commercial Nasal Powder Drug Delivery Device. JOURNAL OF AEROSOL MEDICINE AND

PULMONARY DRUG DELIVERY Volume: 27  
Issue: 6 Pages: A7-A8 Meeting Abstract: P-7

Romana, Bilquis; Batger, Melissa; Prestidge, Clive A.; et al. Expanding the Therapeutic Potential of Statins by Means of Nanotechnology Enabled Drug Delivery Systems. CURRENT TOPICS IN MEDICINAL CHEMISTRY Volume: 14 Issue: 9 Pages: 1182-1193

Tulbah, Alaa S.; Ong, Hui Xin; Colombo, Paolo; et al. Novel Simvastatin Inhalation Formulation and Characterisation. AAPS PHARMSCITECH Volume: 15 Issue: 4 Pages: 956-962.

### 2013

Bacchi, Alessia. Explaining research: how to reach key audiences to advance your work. CRYSTALLOGRAPHY REVIEWS Volume: 19 Issue: 1 Pages: 54-56.

Bacchi, Alessia. X-ray diffraction as a tool in the path from the design of an active pharmaceutical ingredient to the tablet on the shelf. RENDICONTI LINCEI-SCIENZE FISICHE E NATURALI Volume: 24 Supplement: 1 Pages: S109-S114.

Bacchi, Alessia; Bilotti, Ivano; Brillante, Aldo; et al. Raman investigation of polymorphism in 1,1,4,4-tetraphenyl-butadiene. JOURNAL OF RAMAN SPECTROSCOPY Volume: 44 Issue: 6 Pages: 905-908.

Bacchi, Alessia; Cantoni, Giulia; Pelagatti, Paolo. Polymorphs and co-crystal with half-sandwich Ru(II) dimers  $[(\eta(6)\text{-arene})\text{RuX}_2](2)$ . CRYSTENGCOMM Volume: 15 Issue: 34 Pages: 6722-6728.

Balducci, Anna Giulia; Magosso, Enrico; Colombo, Gaia; et al. Agglomerated Oral Dosage Forms of Artemisinin/beta-Cyclodextrin Spray-Dried Primary Microparticles Showing Increased Dissolution Rate and Bioavailability. AAPS PHARMSCITECH Volume: 14 Issue: 3 Pages: 911-918

Barbieri, Stefano; Sonvico, Fabio; Como, Caterina. et al. Lecithin/chitosan controlled release nanopreparations of tamoxifen citrate: Loading, enzyme-trigger release and cell uptake. JOURNAL OF CONTROLLED RELEASE Volume: 167 Issue: 3 Pages: 276-283

Bignardi, Chiara; Mattarozzi, Monica; Penna, Andrea; et al. A Rapid Size-Exclusion Solid-Phase

Extraction Step for Enhanced Sensitivity in Multi-Allergen Determination in Dark Chocolate and Biscuits by Liquid Chromatography-Tandem Mass Spectrometry. FOOD ANALYTICAL METHODS Volume: 6 Issue: 4 Pages: 1144-1152

Carcelli, Mauro; Bacchi, Alessia; Pelagatti, Paolo; et al. Ruthenium arene complexes as HIV-1 integrase strand transfer inhibitors. JOURNAL OF INORGANIC BIOCHEMISTRY Volume: 118 Pages: 74-82.

Cortie, Michael B.; Nafea, Eman H.; Chen, Hui; et al. Nanomedical research in Australia and New Zealand. NANOMEDICINE Volume: 8 Issue: 12 Pages: 1999-2006 Published: DEC

de Araujo, Daniele R.; da Silva, Deyse C.; Barbosa, Raquel M.; et al. Strategies for delivering local anesthetics to the skin: focus on liposomes, solid lipid nanoparticles, hydrogels and patches. EXPERT OPINION ON DRUG DELIVERY Volume: 10 Issue: 11 Pages: 1551-1563.

Di Bari, Maria Teresa; Padula, Cristina; Santi, Patrizia; et al. Dynamics of Water and Small Molecules in Bioadhesive Polymer Films. JOURNAL OF THE PHYSICAL SOCIETY OF JAPAN Volume: 82 Supplement: A: SA021

Franz-Montan, Michelle; Saia Cereda, Cintia Maria; Gaspari, Adele; et al. Liposomal-benzocaine gel formulation: correlation between in vitro assays and in vivo topical anesthesia in volunteers. JOURNAL OF LIPOSOME RESEARCH Volume: 23 Issue: 1 Pages: 54-60.

Heyn, Toby; Anitescu, Mihai; Tasora, Alessandro; et al. Using Krylov subspace and spectral methods for solving complementarity problems in many-body contact dynamics simulation. INTERNATIONAL JOURNAL FOR NUMERICAL METHODS IN ENGINEERING Volume: 95 Issue: 7 Pages: 541-561.

Marra, Fabio; Nicoli, Sara; Padula, Cristina; et al. Amikacin reverse iontophoresis: Optimization of in vitro extraction. INTERNATIONAL JOURNAL OF PHARMACEUTICS Volume: 440 Issue: 2 Pages: 216-220.

Milenkovic, Milica; Bacchi, Alessia; Cantoni, Giulia; et al. Synthesis, characterisation and biological activity of Co(III) complex with the condensation product of 2-(diphenylphosphino)benzaldehyde and ethyl

carbazate. INORGANICA CHIMICA ACTA Volume: 395 Pages: 33-43.

Murtoimaki, Lasse; Vainikka, Tuomas; Pescina, Silvia; et al. Drug adsorption on bovine and porcine sclera studied with streaming potential. JOURNAL OF PHARMACEUTICAL SCIENCES Volume: 102 Issue: 7 Pages: 2264-2272.

Padula, Cristina; Pozzetti, Laura; Traversone, Valeria; et al. In Vitro Evaluation of Mucoadhesive Films for Gingival Administration of Lidocaine. AAPS PHARMSCITECH Volume: 14 Issue: 4 Pages: 1279-1283

Pescina, Silvia; Antopolsky, Maxim; Santi, Patrizia; et al. Effect of iontophoresis on the in vitro trans-scleral transport of three single stranded oligonucleotides. EUROPEAN JOURNAL OF PHARMACEUTICAL SCIENCES Volume: 49 Issue: 2 Pages: 142-147.

Pistara, Venerando; Lombardo, Giuseppe M.; Rescifina, Antonio; et al. Experimental and in silico characterization of a biologically active inosose. STRUCTURAL CHEMISTRY Volume: 24 Issue: 3 Pages: 955-965.

Pupe, Carolina Goncalves; Do Carmo, Flavia Almada; De Sousa, Valeria Pereira; et al. Development of a Doxazosin and Finasteride Transdermal System for Combination Therapy of Benign Prostatic Hyperplasia. JOURNAL OF PHARMACEUTICAL SCIENCES Volume: 102 Issue: 11 Pages: 4057-4064.

Rossi, Alessandra; Buttini, Francesca; Colombo, Paolo; et al. Complex product composition

generates risks for generic substitution also with dosage forms for intravenous administration. INTERNATIONAL JOURNAL OF PHARMACEUTICS Volume: 451 Issue: 1-2 Pages: 50-56

Tasora, Alessandro; Anitescu, Mihai. A complementarity-based rolling friction model for rigid contacts. MECCANICA Volume: 48 Issue: 7 Pages: 1643-1659.

Tulbah, Alaa S.; Ong, Hui Xin; Colombo, Paolo; et al. Simvastatin formulations for pulmonary inflammatory diseases. JOURNAL OF AEROSOL MEDICINE AND PULMONARY DRUG DELIVERY Volume: 27 Issue: 6 Pages: A9-A9 Meeting Abstract: P-12.

Vigliano, Marco; Bianchera, Annalisa; Bettini, Ruggero; et al. Determination of Hyaluronic Acid in a Chitosan-Based Formulation by RP C18 and HILIC LC-ESI-MS: an Evaluation of Matrix Effect. CHROMATOGRAPHIA Volume: 76 Issue: 23-24 Pages: 1761-1766.

Zani, Franca; Veneziani, Cristina; Bazzoni, Elena; et al. Sterilization of corticosteroids for ocular and pulmonary delivery with supercritical carbon dioxide. INTERNATIONAL JOURNAL OF PHARMACEUTICS Volume: 450 Issue: 1-2 Pages: 218-224.

### 3. UO FARMACOLOGIA

L'UO è composta dal laboratorio di Farmacologia Cellulare e quello di Farmacologia e Tossicologia Sperimentale. Il primo offre competenze inerenti allo studio dei processi cellulari coinvolti nell'aterosclerosi. Il secondo offre competenze relative allo svolgimento di indagini farmacologiche, tossicologiche e farmacocinetiche in roditori con specifiche competenze su aspetti legati al tratto gastrointestinale, all'emostasi, a stati infiammatori/algesici, ad alterazioni comportamentali. Oltre alla disponibilità di modelli sperimentali in vivo sono realizzati approfondimenti sui meccanismi d'azione in tessuti, cellule e colture cellulari.

#### Competenze tecnico-scientifiche specifiche

- Studi *in vitro* sul metabolismo intracellulare del colesterolo
- Studi in modelli sperimentali in vivo per la valutazione del trasporto inverso del colesterolo (RCT)
- Studi *ex vivo* sulla capacità del siero animale o umano di promuovere l'efflusso di colesterolo, che rappresenta un parametro di funzionalità delle HDL
- Studio in vivo, *ex vivo* e *in vitro* delle alterazioni funzionali locali e remote associate agli stati infiammatori indotti da ischemia/riperfusion mesenterica, da condizioni di stenosi intestinale e nella colite sperimentale
- Studio delle modulazioni dei processi secretori gastrici e della integrità della barriera mucosale gastrica in modelli sperimentali di ulcere gastro-duodenali acido indotte, prodotte da FANS o da etanolo in roditori
- Valutazione della componente secretoria gastrica e di marker della citoprotezione mucosale in vivo e *in vitro*
- Studio in vivo delle proprietà analgesiche e antiinfiammatorie di prodotti naturali e sintetici e dei loro meccanismi d'azione comprendente la valutazione del rapporto tra dosi efficaci e dosi tollerate (effetti gastrolesivi, effetti sedativi) e la determinazione dei meccanismi sottostanti attraverso test mirati *in vitro*
- Studio degli effetti nutrizionali e protettivi derivanti da somministrazione subacuta e cronica di alimenti complessi, loro componenti, integratori dietetici e alimenti funzionali in roditori mantenuti in condizioni fisiologiche o sottoposti a regimi alimentari modificati. Studio in roditori degli effetti tossicologici subcronici di contaminanti alimentari generati nel corso di processi produttivi.
- Studio in vivo e *ex vivo* della modulazione farmacologica dell'aggregazione piastrinica da parte di nuovi agenti trombolitici/antitrombotici e definizione della tollerabilità e maneggevolezza.
- Sviluppo di ligandi del sistema Eph-ephrin quali potenziali farmaci chemioterapici a bersaglio molecolare mediante test *in vitro* e *in vivo*

#### Brevetti

Nessuno

#### Partecipazione a progetti nazionali di ricerca

- 2014. Ricerca finalizzata del Ministero della Salute. Targeting inflammation in atherosclerosis: role and therapeutic potential of sphingosine 1-phosphate (S1P) and its



receptors. Responsible: Dott. **Francesco Potì**.

- Fondazione Cariplo. Investigating the role of pro-protein convertase subtilisin/kexin type 9 (PCSK9) released from smooth muscle cells on atherogenesis. Responsabile: **Prof. Franco Bernini**.

### Partecipazione a progetti internazionali di ricerca

- 2013. The Medicines Company (Parsippany, NJ, USA). Effect of MDCO-216 on the Secretion of APOE by Macrophages. Responsible: **Dott. Ilenia Zanotti**.
- 2014 Grant from the European Foundation for Alcohol Research (Louvain La Neuve, Belgium). Impact of alcohol consumption on the atheroprotective process of the reverse cholesterol transport. Responsible: **Dott. Ilenia Zanotti**.

### Bibliografia più significativa

#### 2015

Ronda, Nicoletta; Greco, Daniela; Adorni, Maria Pia; et al. Newly Identified Antiatherosclerotic Activity of Methotrexate and Adalimumab Complementary Effects on Lipoprotein Function and Macrophage Cholesterol Metabolism. *ARTHRITIS & RHEUMATOLOGY* Volume: 67 Issue: 5 Pages: 1155-1164  
 Calabresi, Laura; Gomaraschi, Monica; Simonelli, Sara; et al. Insights from inherited HDL disorders. *BIOCHIMICA ET BIOPHYSICA ACTA-MOLECULAR AND CELL BIOLOGY OF LIPIDS* Volume: 1851 Issue: 1 Special Issue: SI Pages: 13-18

#### 2014

Bertoni, Simona; Arcaro, Valentina; Vivo, Valentina; et al. Suppression of inflammatory events associated to intestinal ischemia-reperfusion by 5-HT<sub>1A</sub> blockade in mice. *PHARMACOLOGICAL RESEARCH* Volume: 81 Pages: 17-25  
 Del Bello, Fabio; Bonifazi, Alessandro; Quaglia, Wilma; et al. Mode of interaction of 1,4-dioxane agonists at the M-2 and M-3 muscarinic receptor orthosteric sites. *BIOORGANIC & MEDICINAL CHEMISTRY LETTERS* Volume: 24 Issue: 15 Pages: 3255-3259  
 Di Braccio, Mario; Grossi, Giancarlo; Alfei, Silvana; et al. 1,8-Naphthyridines IX. Potent anti-inflammatory and/or analgesic activity of a new group of substituted 5-amino[1,2,4]triazolo[4,3-a][1,8]naphthyridine-6-carboxamides, of some

their Mannich base derivatives and of one novel substituted 5-amino-10-oxo-10H-pyrimido[1,2-a][1,8]naphthyridine-6-carboxamide derivative. *EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY* Volume: 86 Pages: 394-405.

Greco, Daniela; Favari, Elda; Adorni, Maria Pia; et al. Hydrocortisone directly promotes cholesterol accumulation in macrophages. *ANNALS OF THE RHEUMATIC DISEASES* Volume: 73 Issue: 6 Pages: 1274

Matera, Carlo; Flammini, Lisa; Quadri, Marta; et al. Bis(ammonio)alkane-type agonists of muscarinic acetylcholine receptors: Synthesis, in vitro functional characterization, and in vivo evaluation of their analgesic activity. *EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY* Volume: 75 Pages: 222-232

Pala, Daniele; Scalvini, Laura; Lodola, Alessio; et al. Synthesis and Characterization of New Bivalent Agents as Melatonin- and Histamine H<sub>3</sub>-Ligands. *INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES* Volume: 15 Issue: 9 Pages: 16114-16133

Ronda, Nicoletta; Favari, Elda; Borghi, Maria Orietta; et al. Impaired serum cholesterol efflux capacity in rheumatoid arthritis and systemic lupus erythematosus. *ANNALS OF THE RHEUMATIC DISEASES* Volume: 73 Issue: 3 Pages: 609-615

Vegezzi, Gaia; Al Harraq, Zainab; Levandis, Giovanna; et al. Radiological analysis of gastrointestinal dysmotility in a model of central nervous dopaminergic degeneration:

Comparative study with conventional in vivo techniques in the rat. JOURNAL OF PHARMACOLOGICAL AND TOXICOLOGICAL METHODS Volume: 70 Issue: 2 Pages: 163-169  
Vegezzi, Gaia; Anselmi, Laura; Huynh, Jennifer; et al. Diet-Induced Regulation of Bitter Taste Receptor Subtypes in the Mouse Gastrointestinal Tract. PLOS ONE Volume: 9 Issue: 9 Article Number: e107732

### 2013

Adorni, Maria Pia; Ronda, Nicoletta; Bernini, Franco; et al. Rac1 and Cholesterol Metabolism in Macrophage. JOURNAL OF CARDIOVASCULAR PHARMACOLOGY Volume: 62 Issue: 5 Pages: 418-424

Bertoni, Simona; Sacconi, Francesca; Gatti, Rita; et al. Accommodation and peristalsis are functional responses to obstruction in rat hypertrophic ileum. WORLD JOURNAL OF GASTROENTEROLOGY Volume: 19 Issue: 6 Pages: 846-854

Favari, Elda; Ronda, Nicoletta; Adorni, Maria Pia; et al. ABCA1-dependent serum cholesterol efflux capacity inversely correlates with pulse wave velocity in healthy subjects. JOURNAL OF LIPID RESEARCH Volume: 54 Issue: 1 Pages: 238-243

Franceschini, Guido; Favari, Elda; Calabresi, Laura; et al. Differential effects of fenofibrate and extended-release niacin on high-density lipoprotein particle size distribution and cholesterol efflux capacity in dyslipidemic patients. JOURNAL OF CLINICAL LIPIDOLOGY Volume: 7 Issue: 5 Pages: 414-422

Gobbetti, Thomas; Le Faouder, Pauline; Bertrand, Justine; et al. Polyunsaturated Fatty

Acid Metabolism Signature in Ischemia Differs from Reperfusion in Mouse Intestine. PLOS ONE Volume: 8 Issue: 9 Article Number: e75581

Gomaraschi, Monica; Ossoli, Alice; Favari, Elda; et al. Inflammation impairs eNOS activation by HDL in patients with acute coronary syndrome. CARDIOVASCULAR RESEARCH Volume: 100 Issue: 1 Pages: 36-43

Incerti, Matteo; Tognolini, Massimiliano; Russo, Simonetta; et al. Amino Acid Conjugates of Lithocholic Acid As Antagonists of the EphA2 Receptor. JOURNAL OF MEDICINAL CHEMISTRY Volume: 56 Issue: 7 Pages: 2936-2947

Minicocci, Ilenia; Cantisani, Vito; Poggiogalle, Eleonora; et al. Functional and morphological vascular changes in subjects with familial combined hypolipidemia: An exploratory analysis. INTERNATIONAL JOURNAL OF CARDIOLOGY Volume: 168 Issue: 4 Pages: 4375-4378

Ronda, Nicoletta; Poti, Francesco; Palmisano, Alessandra; et al. Effects of the radiocontrast agent iodixanol on endothelial cell morphology and function VASCULAR PHARMACOLOGY Volume: 58 Issue: 1-2 Pages: 39-47

Russo, Simonetta; Incerti, Matteo; Tognolini, Massimiliano; et al. Synthesis and Structure-Activity Relationships of Amino Acid Conjugates of Cholic Acid as Antagonists of the EphA2 Receptor. MOLECULES Volume: 18 Issue: 10 Pages: 13043-13060

Zanotti, Ilaria; Greco, Daniela; Lusardi, Giulia; et al. Cyclosporine A Impairs the Macrophage Reverse Cholesterol Transport in Mice by Reducing Sterol Fecal Excretion. PLOS ONE Volume: 8 Issue: 8 Article Number: e71572

#### 4. UO MEDICINA E CHIRURGIA SPERIMENTALE

L'UO si occupa, in collaborazione con gruppi nazionali ed internazionali, di studiare terapie a bersaglio molecolare in modelli preclinici di polmone e mammella, e nuove strategie per superare i meccanismi di resistenza a tali trattamenti. Il Coordinatore ed i suoi collaboratori hanno esperienza nel lavoro di gruppo nell'area di ricerca traslazionale del carcinoma polmonare e mammario.

##### Competenze tecnico-scientifiche del personale strutturato

- Saggi di proliferazione e vitalità cellulari (saggi di colonie, MTT, citometria a flusso, incorporazione di timidina)
- Studi di espressione genica, trasduzione del segnale e analisi proteica mediante saggi di Northern blotting, Western- blotting e RT- PCR
- Utilizzo di radioisotopi per misure di trasporto e di metabolismo cellulare
- Studi di meccanismi di morte cellulare e autofagia
- Valutazione del danno al DNA a livello di singole cellule (Halo assay)
- Clonaggio genico, trasfezioni e silenziamento
- Studi su modelli murini

##### Brevetti

Nessuno

##### Partecipazione a progetti nazionali di ricerca

- 2015-2017. Effect of combining AZD9291 with conventional chemotherapy or cetuximab in NSCLC cell lines carrying activating mutations. AstraZeneca SpA 30.000 euro
- 2015 partecipazione al progetto: VATS lobectomy: registro italiano delle lobectomie polmonari eseguite con tecnica mini-invasiva (VATS-Video Assisted Thoracic Surgery).
- 2014-2016. Anti-tumor activity and molecular mechanisms of NVP-BGJ398 in NSCLC: studies in vitro and in xenotransplanted nude mice Novartis 25.000 euro
- 2014-2016. AIRC IG 2013 Novel molecularly targeted approaches in the treatment of squamous cell cancer of the lung. Finanziato da AIRC 360.000 euro
- 2013-2015. Integration of Gefitinib and Conventional Chemotherapy in Preventing or Retarding the Acquisition of Gefitinib Resistance in NSCLC Cell Lines. Astrazeneca Spa 30.000 euro
- 2012-2013. Does the maintenance of gefitinib exert a benefit in NSCLC cell lines become resistant after a prolonged gefitinib treatment? Astrazeneca Spa 30.000 euro
- 2012-2013 Effect of BKM120 and BYL719 alone or in combination with EGFR TK inhibitors in NSCLC cell lines finanziata da Novartis: 20.000 euro
- 2011-2013. Nanosistemi ibridi multifunzionali innovativi per applicazioni biomediche Fondazione Cariparma 750.000 euro.

##### Partecipazione a progetti internazionali di ricerca

- 2015 ETOP Mesoscape: piattaforma europea di studio del mesotelioma pleurico maligno. Partecipazione allo studio specifico: "A Retrospective Cohort Study of phosphorylated

ribosomal protein S6: prevalence and clinical outcomes in patients with mesothelioma in Europe”.

### **Bibliografia più significativa**

#### **2015**

Romeo, Agostino; Tarabella, Giuseppe; D'Angelo, Pasquale; et al. Drug-induced cellular death dynamics monitored by a highly sensitive organic electrochemical system. *BIOSENSORS & BIOELECTRONICS* Volume: 68 Pages: 791-797.

Tiseo M, Gelsomino F, Alfieri RR., et al. FGFR as potential target in the treatment of squamous non small cell lung cancer. *CANCER TREATMENT REVIEWS* 05/2015; DOI:10.1016/j.ctrv.2015.04.011.

#### **2014**

Battistini, Lucia; Burreddu, Paola; Sartori, Andrea; et al. Enhancement of the Uptake and Cytotoxic Activity of Doxorubicin in Cancer Cells by Novel cRGD-Semipeptide-Anchoring Liposomes. *MOLECULAR PHARMACEUTICS* Volume: 11 Issue: 7 Pages: 2280-2293.

Cretella D, (...), Petronini PG, Alfieri RR. Trastuzumab emtansine is active on HER-2 overexpressing NSCLC Cretella, Daniele; Saccani, Francesca; Quaini, Federico; et al. Trastuzumab emtansine is active on HER-2 overexpressing NSCLC cell lines and overcomes gefitinib resistance. *MOLECULAR CANCER* Volume: 13 Article Number: 143.

Fumarola, Claudia; Bonelli, Mara A.; Petronini, Pier Giorgio; et al. Targeting PI3K/AKT/mTOR pathway in non small cell lung cancer. *BIOCHEMICAL PHARMACOLOGY* Volume: 90 Issue: 3 Pages: 197-207.

Tiseo, Marcello; Ippolito, Massimo; Scarlattei, Maura; et al. Predictive and prognostic value of early response assessment using 18FDG-PET in advanced non-small cell lung cancer patients treated with erlotinib. *CANCER CHEMOTHERAPY AND PHARMACOLOGY* Volume: 73 Issue: 2 Pages: 299-307.

#### **2013**

Brigotti, Maurizio; Arfilli, Valentina; Carnicelli, Domenica; et al. Shiga Toxin 1, as DNA Repair Inhibitor, Synergistically Potentiates the Activity

of the Anticancer Drug, Mafosfamide, on Raji Cells. *TOXINS* Volume: 5 Issue: 2 Pages: 431-444.

Corradi, Massimo; Goldoni, Matte; Alinovi, Rossella; et al. YKL-40 and Mesothelin in the Blood of Patients with Malignant Mesothelioma, Lung Cancer and Asbestosis. *ANTICANCER RESEARCH* Volume: 33 Issue: 12 Pages: 5517-5524.

De Filippo, Massimo; Saba, Luca; Concari, Giorgio; et al. Predictive factors of diagnostic accuracy of CT-guided transthoracic fine-needle aspiration for solid noncalcified, subsolid and mixed pulmonary nodules. *RADIOLOGIA MEDICA* Volume: 118 Issue: 7 Pages: 1071-1081.

Fumarola, Claudia; Caffarra, Cristina; La Monica, Silvia; et al. Effects of sorafenib on energy metabolism in breast cancer cells: role of AMPK-mTORC1 signaling. *BREAST CANCER RESEARCH AND TREATMENT* Volume: 141 Issue: 1 Pages: 67-78.

Galvani E, Giovannetti E, Saccani F, Cavazzoni A, Leon LG, Dekker H, Alfieri R, Carmi C, Mor M, Ardizzoni A, Petronini PG, Peters GJ. Molecular mechanisms underlying the antitumor activity of 3-aminopropanamide irreversible inhibitors of the epidermal growth factor receptor in non-small cell lung cancer. *Neoplasia*. 15: 61-72.

Galvani, Elena; Alfieri, Roberta; Giovannetti, Elisa; et al. Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitors: Current Status and Future Perspectives in the Development of Novel Irreversible Inhibitors for the Treatment of Mutant Non-small Cell Lung Cancer. *CURRENT PHARMACEUTICAL DESIGN* Volume: 19 Issue: 5 Pages: 818-832.

Galvani, Elena; Giovannetti, Elisa; Saccani, Francesca; et al. Molecular Mechanisms Underlying the Antitumor Activity of 3-Aminopropanamide Irreversible Inhibitors of the Epidermal Growth Factor Receptor in Non-Small Cell Lung Cancer. *NEOPLASIA* Volume: 15 Issue: 1 Pages: 61.

La Monica S, Caffarra C, Sacconi F, Galvani E, Galetti M, Fumarola C, Bonelli M, Cavazzoni A, Cretella D, Sirangelo R, Gatti R, Tiseo M, Ardizzoni A, Giovannetti E, Petronini PG, Alfieri RR. Gefitinib inhibits invasive phenotype and epithelial-mesenchymal transition in drug-resistant NSCLC cells with MET amplification. PLOS ONE. 8: e78656.

La Monica, Silvia; Caffarra, Cristina; Sacconi, Francesca; et al. Gefitinib Inhibits Invasive Phenotype and Epithelial-Mesenchymal Transition in Drug-Resistant NSCLC Cells with MET Amplification. PLOS ONE Volume: 8 Issue: 10 Article Number: e78656.

Mozzoni, Paola; Banda, Iris; Goldoni, Matteo; et al. Plasma and EBC microRNAs as early biomarkers of non-small-cell lung cancer. BIOMARKERS Volume: 18 Issue: 8 Pages: 679-686.

Negri, Francesca; Bozzetti, Cecilia; Crafa, Pellegrino; et al. Notch and DLL4 expression in

bevacizumab-treated colon cancer patients. CANCER RESEARCH Volume: 73 Issue: 8 Supplement: 1 Meeting Abstract: 4646.

Rocchi, Laura; Alfieri, Roberta R.; Petronini, Pier Giorgio; et al. 5'-Untranslated region of heat shock protein 70 mRNA drives translation under hypertonic conditions. BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS Volume: 431 Issue: 2 Pages: 321-325.

Vacondio, Federica; Carmi, Caterina; Galvani, Elena; et al. Long-lasting inhibition of EGFR autophosphorylation in A549 tumor cells by intracellular accumulation of non-covalent inhibitors. BIOORGANIC & MEDICINAL CHEMISTRY LETTERS Volume: 23 Issue: 19 Pages: 5290-5294.

## 5. UO BIOCHIMICA E BIOLOGIA MOLECOLARE

Questa UO si occupa di i) genomica funzionale e sue applicazioni in ambito farmaceutico/tossicologico; ii) progettazione e realizzazione di prototipi di vaccini peptidici ricombinanti e loro validazione preclinica in modelli animali di patologie amiloidi e infettive.

### Competenze tecnico-scientifiche specifiche

- Genomica funzionale (trascrittomica e analisi fenotipiche su scala genomica) applicata anche alla caratterizzazione di composti di interesse farmaceutico e tossicologico
- Messa a punto di specifici saggi funzionali basati su ingegneria genetica e tecnologia del DNA ricombinante con particolare riferimento alla identificazione di composti xeno-estrogenici (sia agonisti che antagonisti) e alla modellizzazione di patologie amiloidi nell'eucariote modello *Saccharomyces cerevisiae*
- Produzione di proteine ricombinanti in forma detossificata, in particolare immunogeni peptidici ingegnerizzati e dotati di proprietà auto-adiuvanti, utilizzabili come vaccini
- Proteomica e proteomica differenziale di campioni biologici in presenza ed assenza di farmaci
- Caratterizzazione spettroscopica e funzionale di proteine di interesse farmaceutico
- Espressione e purificazione di proteine di interesse farmaceutico
- emoglobine modificate chimicamente come sostituti del sangue
- Analisi chimico cliniche su sangue e plasma
- Progettazione e validazione di ligandi di proteine mediante un approccio integrato computazionale-sperimentale
- Immobilizzazione di enzimi in gel nanoporosi di silice per lo sviluppo di biosensori e bioreattori
- Clonaggio ed espressione di proteine fluorescenti (green fluorescent protein e varianti - GFPs), e di costrutti di fusione tra proteine di interesse biomedico e GFPs, per applicazioni di microscopia di fluorescenza ad alta risoluzione.

### Brevetti

- WO2014140347 (A2) – 2014-09-18. Novel nucleic acid molecules. Dieci Giorgio; Marelli Marcello; Grabstein Kenneth H. Domanda n. WO2014EP55210 20140314

### Partecipazione a progetti nazionali di ricerca

- Gennaio 2013- Gennaio 2016 Progetto AIRC IG 12956. "Broadly protective, low-cost and thermostable anti-human papillomavirus vaccines suitable for mucosal delivery". Prof. **Simone Ottonello**. 180.000 Euro.
- 2012-oggi. Purchased Service Agreement A211985 con il Massachusetts General Hospital, Harvard Medical School. Responsabile scientifico: **Prof. Andrea Mozzarelli**.
- PRIN 2012-2013. "Valutazione dinamica e termodinamica di sistemi proteici: un nuovo approccio NMR a livello di singolo residuo". Responsabile scientifico dell'Unità di ricerca di Parma: Prof. **Rodolfo Berni**. Cofinanziamento MIUR assegnato all'Unità di Ricerca di Parma (erogato nel 2013): 70.368 Euro.

- Giugno 2013-giugno 2016. Programma di Ricerca Regione E.R.-Università. “A tailored approach to the immune-monitoring and clinical management of viral and autoimmune diseases”. Coordinatore: Prof. Carlo Ferrari. Responsabile dell'Unità di Ricerca di Parma: Prof. **Simone Ottonello** (WP2 “New therapeutic strategies based on the identification of novel effective anti-viral compounds”): 248.491 Euro.
- 1/01/2013 - 31/12/2015. Progetto AIRC IG13383 “Carcinogen-induced epigenetic switching in human retroelements: a mechanistic study on benzene effects. Principal investigator: Silvia Fustinoni, Università degli Studi di Milano. Budget complessivo: 330.000 Euro, di cui il 30% (pari a 99.000 Euro) destinato al **Prof. Giorgio Dieci** come “external collaborator”.

### Partecipazione a progetti internazionali di ricerca

- 2014-2016. Biotechnology and Biological Sciences Research Council, UK. “Creating an effective and non-toxic blood substitute”, University of Essex, UK. Responsabile dell'UO di Parma: **Prof. Andrea Mozzarelli**.
- 2015-2017. Medical Research Council, UK. “Engineering a new generation of blood substitutes”, University of Essex, UK. Responsabile dell'UO di Parma: **Prof. Andrea Mozzarelli**.
- 2014-2017. Marie-Curie ITN Project “INTEGRATE”. Università di Parma, Italia: partecipante.
- 2015-2017. Accordo di Cooperazione Scientifica CNR-RFBR (Russia) progetto Comune Mozzarelli/Demidkina su “Engineered methionine gamma-lyase as a novel anticancer drug”, Responsabili scientifici: **Prof. Andrea Mozzarelli**, Prof. Demidkina Tatyana.

### Bibliografia più significativa

#### 2015

Fruscalzo A, Londero Ap, Driul L, Henze A, Tonutti L, Ceraudo M, Zanotti G, Berni R, Schweigert Fj, Raila J. First trimester concentrations of the TTR-RBP4-retinol complex components as early markers of insulin-treated gestational diabetes mellitus. CLIN. CHEM. LAB. MED., In Press.

Cianci M, Folli C, Zonta F, Florio P, Berni R, Zanotti G. Structural evidence for asymmetric ligand binding to transthyretin. ACTA D, BIOLOGICAL CRYSTALLOGRAPHY. In Press

Campanini, Barbara; Pieroni, Marco; Raboni, Samanta; et al. Inhibitors of the Sulfur Assimilation Pathway in Bacterial Pathogens as Enhancers of Antibiotic Therapy. CURRENT MEDICINAL CHEMISTRY Volume: 22 Issue: 2 Pages: 187-213.

Conti, Anastasia; Carnevali, Davide; Bollati, Valentina; et al. Identification of RNA

polymerase III-transcribed Alu loci by computational screening of RNA-Seq data. NUCLEIC ACIDS RESEARCH Volume: 43 Issue: 2 Pages: 817-835

Fraccia, Tommaso P.; Smith, Gregory P.; Zanchetta, Giuliano; et al. Abiotic ligation of DNA oligomers templated by their liquid crystal ordering. NATURE COMMUNICATIONS Volume: 6 Article Number: 6424.

Gallego-Yerga, Laura; Lomazzi, Michela; Franceschi, Valentina; et al. Cyclodextrin- and calixarene-based polycationic amphiphiles as gene delivery systems: a structure-activity relationship study. ORGANIC & BIOMOLECULAR CHEMISTRY Volume: 13 Issue: 6 Pages: 1708-1723.

Marchetti, Marialaura; Bruno, Stefano; Campanini, Barbara; et al. Regulation of human serine racemase activity and dynamics by

halides, ATP and malonate. AMINO ACIDS  
Volume: 47 Issue: 1 Pages: 163-173.

#### 2014.

Branca, Caterina; Sarnico, Ilenia; Ruotolo, Roberta; et al. Pharmacological targeting of the beta-amyloid precursor protein intracellular domain. SCIENTIFIC REPORTS Volume: 4 Article Number: 4618

Bruno, Stefano; Pinto, Andrea; Paredi, Gianluca; et al. Discovery of Covalent Inhibitors of Glyceraldehyde-3-phosphate Dehydrogenase, A Target for the Treatment of Malaria. JOURNAL OF MEDICINAL CHEMISTRY Volume: 57 Issue: 17 Pages: 7465-7471

Canali, Elena; Bolchi, Angelo; Spagnoli, Gloria; et al. A high-performance thioredoxin-based scaffold for peptide immunogen construction: proof-of-concept testing with a human papillomavirus epitope. SCIENTIFIC REPORTS Volume: 4 Article Number: 4729

Fiscaro, Emilia; Compari, Carlotta; Bacciottini, Franco; et al. Nonviral Gene Delivery: Gemini Bispyridinium Surfactant-Based DNA Nanoparticles. JOURNAL OF PHYSICAL CHEMISTRY B Volume: 118 Issue: 46 Pages: 13183-13191.

Franceschi, Valentina; Jacca, Sarah; Sassu, Elena L.; et al. Generation and Characterization of the First Immortalized Alpaca Cell Line Suitable for Diagnostic and Immunization Studies. PLOS ONE Volume: 9 Issue: 8 Article Number: e105643.

Franceschi, Valentina; Stellari, Fabio Franco; Mangia, Carlo; et al. In Vivo Image Analysis of BoHV-4-Based Vector in Mice. PLOS ONE Volume: 9 Issue: 4 Article Number: e95779

Jacca, Sarah; Franceschi, Valentina; Agosti, Mattia; et al. Interferon Gamma-Mediated BoHV-4 Replication Restriction in Bovine Endometrial Stromal Cells Is Host IDO1 Gene Expression Independent and BoHV-4 IE2 Gene Expression Dependent. BIOLOGY OF REPRODUCTION Volume: 91 Issue: 5 Article Number: 112.

Mantile, Francesca; Trovato, Maria; Santoni, Andrea; et al. Alum and Squalene-Oil-in-Water Emulsion Enhance the Titer and Avidity of Anti-A beta Antibodies Induced by Multimeric Protein Antigen (1-11)E2, Preserving the Igg1-Skewed

Isotype Distribution. PLOS ONE Volume: 9 Issue: 7 Article Number: e101474

Micalella, Chiara; Caglio, Raffaella; Mozzarelli, Andrea; et al. Ormosil gels doped with engineered catechol 1,2 dioxygenases for chlorocatechol bioremediation. BIOTECHNOLOGY AND APPLIED BIOCHEMISTRY Volume: 61 Issue: 3 Pages: 297-303.

Montanini, Barbara; Chen, Pao-Yang; Morselli, Marco; et al. Non-exhaustive DNA methylation-mediated transposon silencing in the black truffle genome, a complex fungal genome with massive repeat element content. GENOME BIOLOGY Volume: 15 Issue: 7 Article Number: 411

Nakagawa, Akito; Lui, Francine E.; Wassaf, Dina; et al. Identification of a Small Molecule that Increases Hemoglobin Oxygen Affinity and Reduces SS Erythrocyte Sickling. ACS CHEMICAL BIOLOGY Volume: 9 Issue: 10 Pages: 2318-2325.

Pellegrino, Sara; Ronda, Luca; Annoni, Chiara; et al. Molecular insights into dimerization inhibition of c-Maf transcription factor. BIOCHIMICA ET BIOPHYSICA ACTA-PROTEINS AND PROTEOMICS Volume: 1844 Issue: 12 Pages: 2108-2115.

Puppo A, Cesi G, Marrocco E, Piccolo P, Jacca S, Shayakhmetov DM, Parks RJ, Davidson BL, Colloca S, Brunetti-Pierri N, Ng P, Donofrio G, Auricchio A. Retinal transduction profiles by high-capacity viral vectors. Gene Ther. 2014 Jul 3. doi: 10.1038/gt.2014.57.

Ruotolo, Roberta; Calani, Luca; Brighenti, Furio; et al. Glucuronidation does not suppress the estrogenic activity of quercetin in yeast and human breast cancer cell model systems. ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS Volume: 559 Pages: 62-67

Seitz, Hanna; Canali, Elena; Ribeiro-Mueller, Lis; et al. A three component mix of thioredoxin-L2 antigens elicits broadly neutralizing responses against oncogenic human papillomaviruses. VACCINE Volume: 32 Issue: 22 Pages: 2610-2617

Spyrakakis, Francesca; Cellini, Barbara; Bruno, Stefano; et al. Targeting Cystalytin, a Virulence Factor of Treponema denticola-Supported



Periodontitis. CHEMMEDCHEM Volume: 9 Issue: 7 Pages: 1501-1511.

Stellari, Fabio Franco; Lavrentiadou, Sophia; Ruscitti, Francesca; et al. Enlightened Mannheimia haemolytica lung inflammation in bovinized mice. VETERINARY RESEARCH Volume: 45 Article Number: 8

Storti, Paola; Donofrio, Gaetano; Marchica, Valentina; et al. Galectin-1 Is Highly Expressed By Myeloma Cells and the Bone Marrow Microenvironment and Its Suppression Delineates a New Therapeutic in Vitro and in Vivo Strategy in Multiple Myeloma. BLOOD Volume: 124 Issue: 21.

Viappiani, Cristiano; Abbruzzetti, Stefania; Ronda, Luca; et al. Experimental basis for a new allosteric model for multisubunit proteins. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA Volume: 111 Issue: 35 Pages: 12758-12763

### 2013

Ahmed, Mostafa H.; Habtemariam, Mesay; Safo, Martin K.; et al. Unintended consequences? Water molecules at biological and crystallographic protein-protein interfaces. COMPUTATIONAL BIOLOGY AND CHEMISTRY Volume: 47 Pages: 126-141

Bagnacani, Valentina; Franceschi, Valentina; Bassi, Michele; et al. Arginine clustering on calix[4]arene macrocycles for improved cell penetration and DNA delivery. NATURE COMMUNICATIONS Volume: 4 Article Number: 1721.

Bertolotti, Luigi; Rosamilia, Alfonso; Profiti, Margherita; et al. Characterization of caprine herpesvirus 1 (CpHV1) glycoprotein E and glycoprotein I ectodomains expressed in mammalian cells. VETERINARY MICROBIOLOGY Volume: 164 Issue: 3-4 Pages: 222-228.

Bolzoni M, Donofrio G, Storti P, Guasco D, Toscani D, Lazzaretti M, Bonomini S, Agnelli L, Capocefalo A, Palma BD, Neri A, Nicolini F, Lisignoli G, Russo F, Colla S, Aversa F, Giuliani N. Myeloma cells inhibit non-canonical Wnt co-receptor Ror2 expression in human bone marrow osteoprogenitor cells: effect of Wnt5a/Ror2 pathway activation on the

osteogenic differentiation impairment induced by myeloma cells. Leukemia. 27(2):451-63.

Campanini, Barbara; Bettati, Stefano; di Salvo, Martino Luigi; et al. Asymmetry of the Active Site Loop Conformation between Subunits of Glutamate-1-semialdehyde Aminomutase in Solution. BIOMED RESEARCH INTERNATIONAL Article Number: 353270.

Campanini, Barbara; Pioselli, Barbara; Raboni, Samanta; et al. Role of histidine 148 in stability and dynamics of a highly fluorescent GFP variant. BIOCHIMICA ET BIOPHYSICA ACTA-PROTEINS AND PROTEOMICS Volume: 1834 Issue: 4 Pages: 770-779.

Campanini, Barbara; Spyrikis, Francesca; Peracchi, Alessio; et al. Serine racemase: a key player in neuron activity and in neuropathologies. FRONTIERS IN BIOSCIENCE-LANDMARK Volume: 18 Pages: 1112-1128

Capocefalo, Antonio; Mangia, Carlo; Franceschi, Valentina; et al. Efficient heterologous antigen gene delivery and expression by a replication-attenuated BoHV-4-based vaccine vector. VACCINE Volume: 31 Issue: 37 Pages: 3906-3914.

Cavazzini, Davide; Meschi, Francesca; Corsini, Romina; et al. Autoproteolytic Activation of a Symbiosis-regulated Truffle Phospholipase A(2). JOURNAL OF BIOLOGICAL CHEMISTRY Volume: 288 Issue: 3 Pages: 1533-1547.

Ciarlo, Eleonora; Massone, Sara; Penna, Ilaria; et al. An intronic ncRNA-dependent regulation of SORL1 expression affecting A beta formation is upregulated in post-mortem Alzheimer's disease brain samples. DISEASE MODELS & MECHANISMS Volume: 6 Issue: 2 Pages: 424-433.

Dieci, Giorgio; Bosio, Maria Cristina; Fermi, Beatrice; et al. Transcription reinitiation by RNA polymerase III. BIOCHIMICA ET BIOPHYSICA ACTA-GENE REGULATORY MECHANISMS Volume: 1829 Issue: 3-4 Special Issue: SI Pages: 331-341.

Dieci, Giorgio; Conti, Anastasia; Pagano, Aldo; et al. Identification of RNA polymerase III-transcribed genes in eukaryotic genomes. BIOCHIMICA ET BIOPHYSICA ACTA-GENE REGULATORY MECHANISMS Volume: 1829 Issue: 3-4. Pages: 296-305.

Donofrio, Gaetano; Franceschi, Valentina; Lovero, Angela; et al. Clinical Protection of Goats against CpHV-1 Induced Genital Disease with a BoHV-4-Based Vector Expressing CpHV-1 gD. PLOS ONE Volume: 8 Issue: 1 Article Number: e52758.

Franceschi, Valentina; Capocefalo, Antonio; Cavirani, Sandro; et al. Bovine herpesvirus 4 glycoprotein B is indispensable for lytic replication and irreplaceable by VSVg. BMC VETERINARY RESEARCH Volume: 9 Article Number: 6.

Gabba, Matteo; Abbruzzetti, Stefania; Spyraakis, Francesca; et al. CO Rebinding Kinetics and Molecular Dynamics Simulations Highlight Dynamic Regulation of Internal Cavities in Human Cytoglobin. PLOS ONE Volume: 8 Issue: 1 Article Number: e49770

Jacca, Sarah; Franceschi, Valentina; Colagiorgi, Angelo; et al. Bovine Endometrial Stromal Cells Support Tumor Necrosis Factor Alpha-Induced Bovine Herpesvirus Type 4 Enhanced Replication. BIOLOGY OF REPRODUCTION Volume: 88 Issue: 5 Article Number: 135.

Marchetti, Maria Laura; Bruno, Stefano; Campanini, Barbara; et al. ATP binding to human serine racemase is cooperative and modulated by glycine. FEBS JOURNAL Volume: 280 Issue: 22 Pages: 5853-5863.

Mazzera, Laura; Lombardi, Guerino; Abeltino, Manuela; et al. Aurora and IKK kinases cooperatively interact to protect multiple myeloma cells from Apo2L/TRAIL. BLOOD Volume: 122 Issue: 15 Pages: 2641-2653.

Mozzarelli, Andrea; Viappiani, Cristiano. Oxygen binding and sensing proteins Preface. BIOCHIMICA ET BIOPHYSICA ACTA-PROTEINS AND PROTEOMICS Volume: 1834 Issue: 9 Special Issue: SI Pages: 1683.

Paredi, Gianluca; Sentandreu, Miguel-Angel; Mozzarelli, Andrea; et al. Muscle and meat: New horizons and applications for proteomics on a farm to fork perspective. JOURNAL OF PROTEOMICS Volume: 88 Pages: 58-82.

Penna, Ilaria; Vassallo, Irene; Nizzari, Mario; et al. A novel snRNA-like transcript affects amyloidogenesis and cell cycle progression through perturbation of Fe65L1 (APBB2) alternative splicing. BIOCHIMICA ET

BIOPHYSICA ACTA-MOLECULAR CELL RESEARCH Volume: 1833 Issue: 6 Pages: 1511-1526.

Ronda L, Bettati S, Henry ER, Kashav T, Sanders JM, Royer WE, Mozzarelli A. Tertiary and Quaternary Allostery in Tetrameric Hemoglobin from *Scapharca inaequalvis*. Biochemistry, 2013, 52, 2108–2117.

Ronda, Luca; Bettati, Stefano; Henry, Eric R.; et al. Tertiary and Quaternary Allostery in Tetrameric Hemoglobin from *Scapharca inaequalvis*. BIOCHEMISTRY Volume: 52 Issue: 12 Pages: 2108-2117.

Ronda, Luca; Bruno, Stefano; Bettati, Stefano. Tertiary and quaternary effects in the allosteric regulation of animal hemoglobins. BIOCHIMICA ET BIOPHYSICA ACTA-PROTEINS AND PROTEOMICS Volume: 1834 Issue: 9 Special Issue: SI Pages: 1860-1872

Ronda, Luca; Merlino, Antonello; Bettati, Stefano; et al. Role of tertiary structures on the Root effect in fish hemoglobins. BIOCHIMICA ET BIOPHYSICA ACTA-PROTEINS AND PROTEOMICS Volume: 1834 Issue: 9 Special Issue: SI Pages: 1885-1893.

Ronda, Luca; Mozzarelli, Andrea; Aloe, Rosalia; et al. Development of a novel, hemolysis-resistant reagent for assessment of alpha-amylase in biological fluids. CLINICAL CHEMISTRY AND LABORATORY MEDICINE Volume: 51 Issue: 7 Pages: 1409-1415

Ruotolo R., Calani L., Fietta E., Brighenti F., Crozier A., Meda C., Maggi A., Ottonello S., Del Rio D. Anti-estrogenic activity of a human resveratrol metabolite. Nutr Metab Cardiovasc Dis 1-7. ISSN:0939-4753

Seitz, Hanna; Danthony, Tatiana; Burkart, Frank; et al. Influence of Oxidation and Multimerization on the Immunogenicity of a Thioredoxin-L2 Prophylactic Papillomavirus Vaccine. CLINICAL AND VACCINE IMMUNOLOGY Volume: 20 Issue: 7 Pages: 1061-1069

Singh, Ratna; Spyraakis, Francesca; Cozzini, Pietro; et al. Chemogenomics of pyridoxal 5'-phosphate dependent enzymes. JOURNAL OF ENZYME INHIBITION AND MEDICINAL CHEMISTRY Volume: 28 Issue: 1 Pages: 183-194.

Sivilia, Sandra; Lorenzini, Luca; Giuliani, Alessandro; et al. Multi-target action of the novel

anti-Alzheimer compound CHF5074: in vivo study of long term treatment in Tg2576 mice. BMC NEUROSCIENCE Volume: 14 Article Number: 44

Spyrakakis, Francesca; Felici, Paolo; Bayden, Alexander S.; et al. Fine tuning of the active site modulates specificity in the interaction of O-acetylserine sulfhydrylase isozymes with serine acetyltransferase. BIOCHIMICA ET BIOPHYSICA ACTA-PROTEINS AND PROTEOMICS Volume: 1834 Issue: 1 Pages: 169-181

Spyrakakis, Francesca; Singh, Ratna; Cozzini, Pietro; et al. Isozyme-Specific Ligands for O-acetylserine sulfhydrylase, a Novel Antibiotic Target. PLOS ONE Volume: 8 Issue: 10 Article Number: e77558

Storti P, Bolzoni M, Donofrio G, Airoidi I, Guasco D, Toscani D, Martella E, Lazzaretti M, Mancini C, Agnelli L, Patrene K, Maïga S, Franceschi V, Colla S, Anderson J, Neri A, Amiot M, Aversa F, Roodman GD, Giuliani N. Hypoxia-inducible factor (hif)-1 $\alpha$  suppression in myeloma cells blocks tumoral growth in vivo inhibiting angiogenesis and bone destruction. Leukemia Jan 24.

Turroni, Francesca; Serafini, Fausta; Foroni, Elena; et al. Role of sortase-dependent pili of Bifidobacterium bifidum PRL2010 in modulating bacterium-host interactions. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA Volume: 110 Issue: 27 Pages: 11151-11156.

Zanotti, Giuseppe; Cendron, Laura; Folli, Claudia; et al. Structural evidence for native state stabilization of a conformationally labile amyloidogenic transthyretin variant by fibrillogenesis inhibitors. FEBS LETTERS Volume: 587 Issue: 15 Pages: 2325-2331.

**Tab. 1.** La tabella descrive le commesse svolte a partire dal 2013 o in anni precedenti ed ancora in atto durante il periodo coperto dal presente manuale. Sono indicate la data di inizio e fine del contratto, le UO, il responsabile di BPN-T, la tipologia di attività svolta, il committente e il valore della commessa (in migliaia di euro).

Inizio	Fine	UO	Responsabile		Attività svolta	Committente	Valore
			BPN-T				
20110701	20141231	DDTP	Prof. P. Colombo		consulenza farmaceutica	Consorzio TEFARCO innova	37
20120227	20130331	BBM	Prof. A. Mozzarelli		espressione di proteine	Chiesi 3/12	40
20120416	20140102	DDTP	Prof. R. Bettini		consulenza farmaceutica	Tecnimede	120
20121024	20130223	BBM	Prof. A. Mozzarelli		caratterizzazione proteine	Chiesi 10/12	4
20121101	20131031	BBM	prof. A. Bolchi		ricerca farmaceutica	Chiesi 11/12	20
20121114	20130313	DDTP	Prof. R. Bettini		ricerca farmaceutica	Alfa Wassermann 14/12	20
20121128	20130615	DDTP	Prof. R. Bettini		ricerca farmaceutica	Chiesi 15/12	27
20130208	20130408	DD	Prof. M. Mor		analisi interazioni farmaceutiche	Ceva	2
20130405	20130605	DDTP	Prof. R. Bettini		analisi farmaceutiche	Chiesi 3/13	12
20130412	20130812	DDTP	Prof. R. Bettini		sviluppo farmaceutico	MDT int'l sa 6/13	13
20130417	20130717	DDTP	Prof. R. Bettini		test di dissoluzione	Alfa Wasserman 2/13	15
20130430	20130531	DDTP	Prof. R. Bettini		analisi farmaceutiche	Alfa Wasserman 4/13	5
20130430	20130531	DD	Prof. M. Mor		valutazioni farmaceutiche	Alchemy	6
20130430	20140530	DDTP	Prof. R. Bettini		analisi farmaceutiche	Alfa Wasserman 11/13	12
20130612	20131112	DDTP	Prof. R. Bettini		sviluppo preformulativo	Chiesi 8/13	30
20130624	20140724	DDTP	Prof. R. Bettini		analisi preformulazione	MDT int'l sa 7/13	3
20130920	20140520	F	Prof. F. Bernini		valutazione farmacologiche	Rottapharm 9/13	48
20130923	20150322	BBM	Prof. Mozzarelli		analisi	Chiesi 10/13	40
						Consorzio TEFARCO Innova (129)	
20131015	20131215	DDTP	Prof. P. Santi		studi rilascio del farmaco	12/13	10
						Consorzio TEFARCO Innova (130)	
20131015	20131215	DDTP	Prof. P. Santi		studi di rilascio del farmaco	13/13	10
					purificazione e metodi		
20140107	20140707	BBM	Prof. A. Mozzarelli		computazionali	Chiesi 1/14	25
20140219	20141219	DDTP	Prof. R. Bettini		sviluppo e convalide	Medinova 2/14	28

				studi di metodiche di		
20140227	20150226	DDTP	Prof. A. Bacchi	crystallization	Chiesi 3/14	30
20140430	20150731	DDTP	Prof. R. Bettini	development of new formulations	Medinova 4/14	65
20140609	20150608	BBM	Prof. A. Bolchi	development of formulations	Chiesi 5/14	18
20140701	20141231	DD	Prof. G. Costantino	analysis	Dompe 6/14	25
20140901	20141030	DDTP	Dr F. Buttini	analysis	Chiesi 7/14	7
20140925	20141030	DDTP	Dr F. Buttini	analysis	Chiesi 9/14	5
20141006	20141231	DDTP	Dr F. Buttini	aerodynamic performance of powders	Chiesi 8/14	12
20141125	20141220	DDTP	Dr F. Buttini	analysis	Chiesi 10/14	7
20141215	20151231	BBM	Prof. A. Mozzarelli	analysis	Chiesi 11/14	40
20141215	20150401	BBM	Prof. G. Donofrio	stem cell characterization	Chiesi 1/15	30
20150204	20150430	DDTP	Prof. R. Bettini	aerosolization studies	Hikma Italia 2/15	18
20150416	20160416	DDTP	Prof. R. Bettini	compression studies	IMA Active 3/15	65