UNIVERSITÀ DI PARMA

Department of Food and Drug Sciences

ULLA ExCo Meeting

Copenhagen November 16th, 2018

Food & Drug Department

- Est. in 2017.

- Study of **medicinal products and foods**, is based on the consideration that their scope of action is common: the health and well-being of humans and animals.

- The development of food and drugs the understanding of their mechanism of action and their formulation require an interdisciplinary approach that ultimately aims at the well-being of the person obtained through **balanced nutrition** with products that deliver vital substances to life, **nutraceutical products** that can prevent some pathologies, and **therapeutic treatments** that allow you to recover from a state of illness.

PHARMACY BUILDING
Parco Area delle Scienze 27/a - CAMPUS

Research Organisation (Pharma Side)

5 main areas

- Bio-organic Synthesis
- Medicinal Chemistry and Drug Design
- Drug Delivery and Pharmaceutical Technology
- Experimental Pharmacology
- Biochemistry and biotechnology

Bio-organic Synthesis group

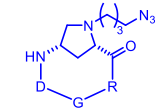
Franca Zanardi (Associate Professor)
Lucia Battistini (Associate Professor)
Claudio Curti (Associate Professor)
Andrea Sartori (Associate Professor)

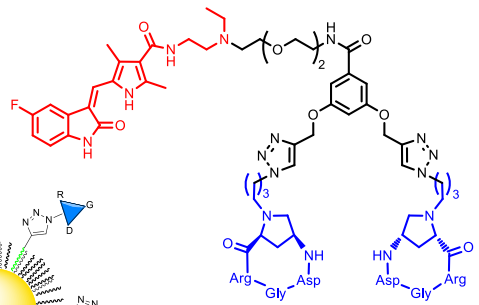
Research topics

- Lab-scale asymmetric synthesis of chiral organic molecules
- Purification and analysis of enantiopure compounds
- In solution and solid-phase synthesis of small peptides, cyclopeptides and peptidomimetics
- Synthesis of covalent conjugates (peptide-small molecule drug ,peptide-lipide, peptide-fluorescent agent, peptide-chelating unit)
- Radiosynthesis (collaboration with Nuclear Medicine Unit, Parma Hospital)
- Fabrication and characterization of liposomes and gold nanoparticles
- Purification by chromatografic techniques (automated flash, HPLC)
- Spectroscopic characterization (1D and 2D-NMR, IR, CD, mass spectrometry)

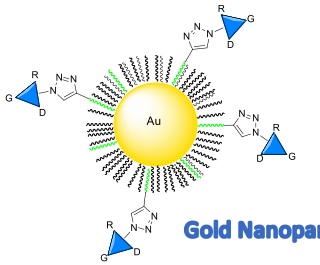
Main Active Projects

Synthesis of Multifunctional Peptidomimetics Targeting Integrins for Drug Delivery and Diagnosis



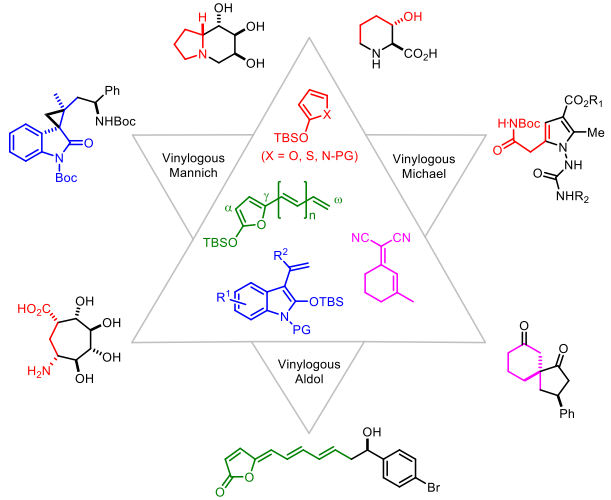


Sunitinib Conjugate

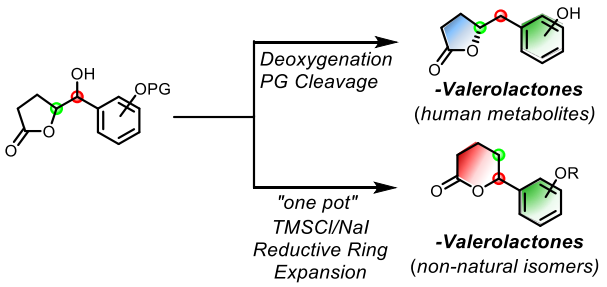


Gold Nanoparticles

Introduction of Novel Chemical Methods in Asymmetric Synthesis to Selectively Access Molecular Diversity in the Domain of Medicinally-Relevant Small Molecules



Asymmetric Synthesis of Chiral Metabolites of Polyphenols and Liver Phase II-related Conjugates



P4T
Probes for Targets

Gabriele Costantino (Professor)
Marco Radi (Associate Professor)
Marco Pieroni (Assistant Professor)
Giannamaria Annunziato (Post doc)

Involved in developing novel small-molecule probes for a wide range of therapeutic targets by combining molecular modeling and combinatorial chemistry approaches.

Main therapeutic areas:

Anti-infectives
Anti tubercular agents
Nutraceutics
Molecular modeling
Combinatorial chemistry

Main projects funded

INTEGRATE is a European Project aiming at the discovery of novel targets for the development of new antibacterial drugs.
The project is part of Marie-Curie actions of Horizon 2020 and is coordinated by prof. G. Costantino.

Main ongoing collaborations

UNIVERSIDADE NOVA DE LISBOA	*Prof Miguel Viveiros*
JOHNS HOPKINS UNIVERSITY	*Prof William Bishai*
UNIVERSITY OF CAMBRIDGE	*Prof Martin Welch*
UNIVERSITÀ DEGLI STUDI FIRENZE NEUROFARBA DIPARTIMENTO DI NEUROSCIENZE, PSICOLOGIA, AREA DEL FARMACO E SALUTE DEL BAMBINO	*Prof Caludiu Supuran*
aptuit	*Dr. Antonio Felici*
Fraunhofer IME	*Dr Philip Gribbon*

Drug Design & Discovery Group

Drug Design

Marco Mor (Professor)
Silvia Rivara (Associate Professor)
Alessio Lodola (Associate Professor)

Pharmaceutical Analysis

Federica Vacondio (Associate Professor)
Claudia Silvia (Associate Professor)

Synthesis of Compounds

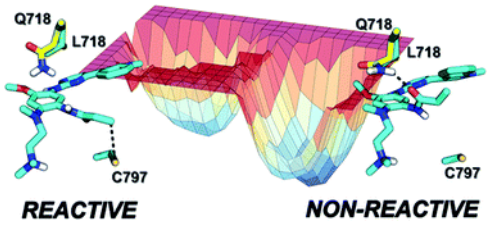
Riccardo Castelli (Assistant Professor)

Research areas

- **Modulators of the Endocannabinoid System**
  - Design and SAR analysis of Fatty Acid Amide Hydrolase (FAAH) inhibitors
  - Design and synthesis of N-acylethanolamine acid amidase (NAAA) inhibitors
  - Design and synthesis of Monoglyceride Lipase (MGL) inhibitors
  - Design and SAR analysis of NAPE-PLD inhibitors

- **GPCR ligands**
  - Design and QSAR analysis of MT_1 and MT_2 melatonin receptor ligands

- **Kinase inhibitors**
  - Design and synthesis of covalent inhibitors of EGFR
  - Design and synthesis of covalent inhibitors of FGFR



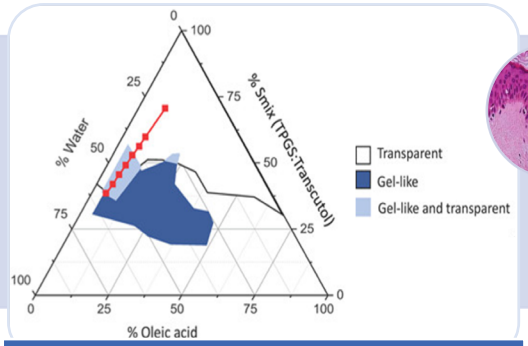
- **Protein-Protein Interaction Inhibitors**
  - Design and synthesis of small molecules acting as FGF traps
  - Design and synthesis of EphA2 antagonists

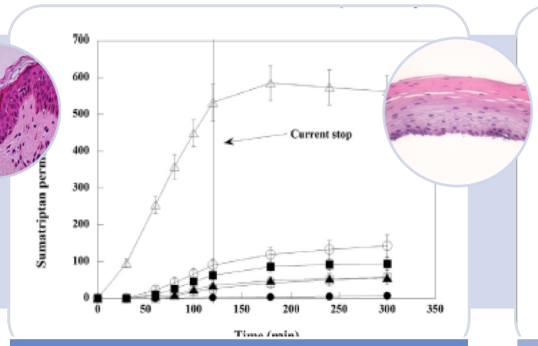
Skin, ocular and buccal drug delivery

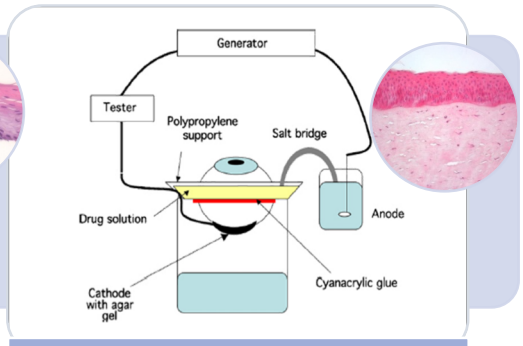
- Patrizia Santi (Professor)
- Sara Nicoli (Associate Professor)
- Cristina Padula (Assistant Professor)
- Silvia Pescina (Assistant Professor)

- International collaborations (5 y)
  - University of Helsinki, Finland
  - Universidade da Região da Campanha, URCAMP, Brazil
  - Universidade Federal do Rio de Janeiro (IMA/UFRJ), Brazil
  - Ege University, Izmir, Turkey
  - Universidade de Santiago de Compostela, Spain
  - Federal University of ABC, São Paulo, Brazil

Main research subjects







Dermal and Transdermal Delivery

Main model: Porcine ear skin

Ex1. microemulsions for imiquimod dermal delivery
Ex2. transdermal iontophoresis for enhanced drug delivery
Ex3. bioadhesive patch for dermal and transdermal delivery

Buccal Delivery

Main model: Porcine esophageal epithelium

Ex1. sumatriptan succinate buccal iontophoresis
Ex2. microemulsions for triamcinolone acetonide delivery

Ocular Delivery

for anterior and posterior segment

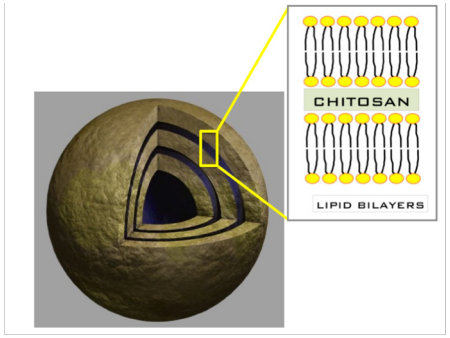
Main model: Porcine eye

Ex1. influence of the vehicle on stability and transcorneal diffusion of cysteamine
Ex2. iontoporetic transcleral delivery of mAb and oligonuceotides

Drug Delivery and pharmaceutical technology

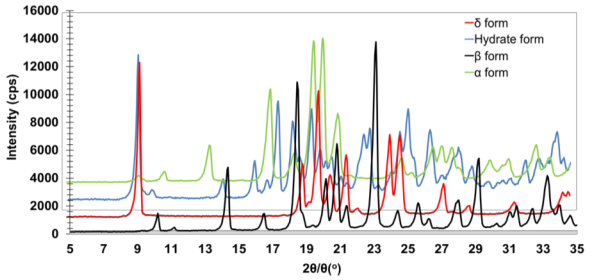
Ruggero Bettini, Professor
Lisa Elviri, Associate Professor
Fabio Sonvico, Associate Professor
Francesca Buttini, Associate Professor
Alessandra Rossi, Assistant Professor

Post doc
Annalisa Bianchera
Adryana Rocha Clementino
Irene Rossi



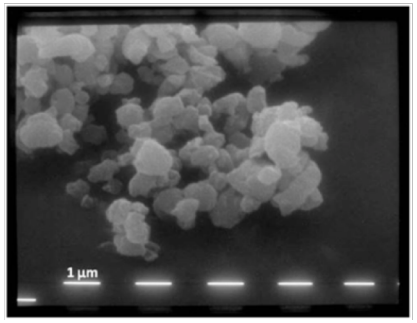
Research topics

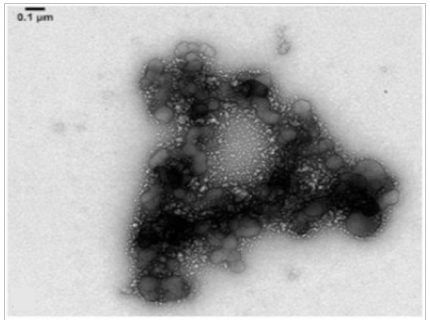
Nasal and pulmonary drug delivery (small molecules peptides and proteins)
Oral controlled drug delivery (poorly absorbed compounds, local delivery)
Nose to brain delivery



Approaches

Solid state manipulation
Nanoparticulate systems
Nonosystems → free flowing powders





COMBINATION of 3D TECHNOLOGY and BIOMATERIAL to DEVELOP MEDICAL DEVICES for TISSUE REGENERATION

DIFFERENT COMPOSITION

3D printing of a wide rage of natural and synthetic polymers

(i.e. hyaluronic acid, alginate, collagen, fibroin..)

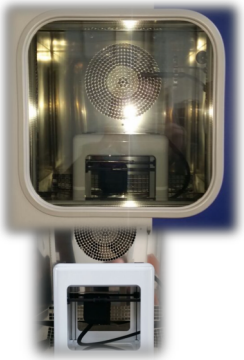
ACTIVE COMPOUNDS

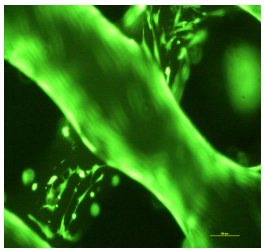
Inclusion of a variety natural active compounds

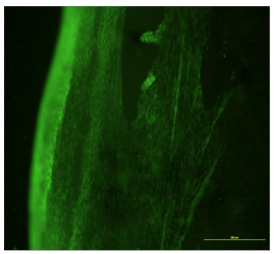
(i.e. antioxidants, lipids, oils, vitamins etc.)

DRUG DELIVERY SYSTEMS

Development of localized controlled drug delivery systems







Experimental pharmacology

Elisabetta Barocelli (Professor)
Vigilio Ballabeni (Associate Professor)
Massimiliano Tognolini (Associate Professor)
Simona Bertoni (Assistant Professor)

Research Topics

- Study of the local and systemic effects of drugs delivered by pulmonary inhalation
- Pharmacokinetics and safety pharmacology studies of new potential drugs and formulations

Main research

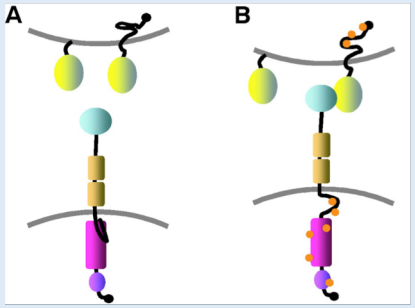
Gastric secreto-motor disorders

Intestinal motor disorders
IBS

Intestinal and extra-intestinal inflammatory disorders
IBD

in vitro and *in vivo* studies on GI effects of new potential drugs, natural products and probiotics
Evaluation of gut-brain axis

Discovery and development of new protein-protein Inhibitors of Eph-ephrin interaction



✓Binding assay
✓In vitro studies on cell cycle, signal transduction, cell proliferation and migration, angiogenesis
✓In vivo studies in models of cancer, diabetes, pain, blood clotting disorders

Lipid pharmacology

Lipid metabolism as a pharmacological/nutraceuti cal target for the treatment of cardiovascular, autoimmune, pulmonary and neurodegenerative diseases

- Franco Bernini, Professor
- Nicoletta Ronda, Assistant Professor
- Ilaria Zanotti, Assistant Professor
- Francesca Zimetti, Assistant Professor
- Maria Pia Adorni, Post-doc

Pleiotropic effects of PCSK9

Association of HDL functionality with atherosclerosis and Alzheimer

Role of diet/microbiota in health and disease

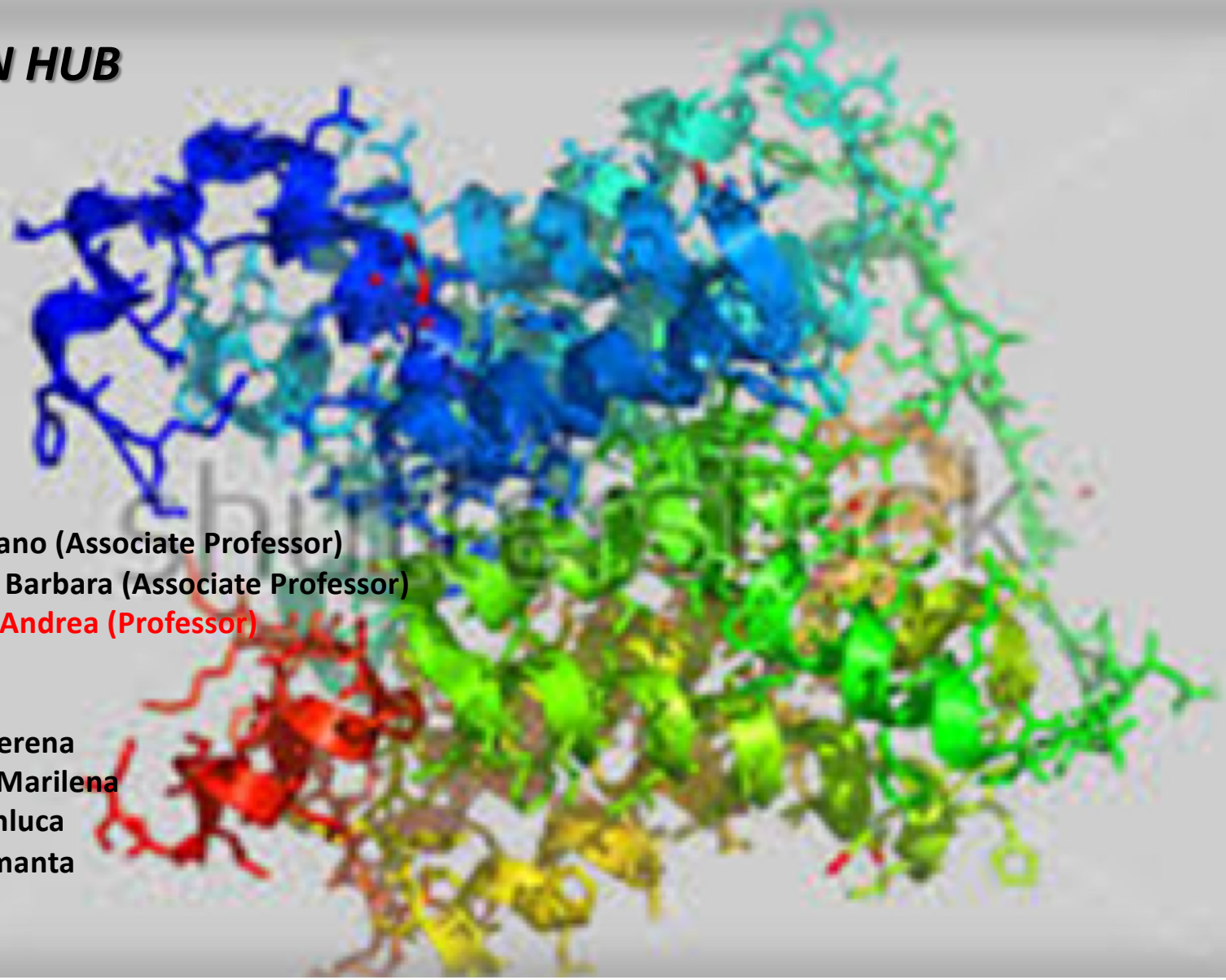
Pharmacological/Nutraceutical modulation of cholesterol metabolism

In vitro studies (cell cultures)
- Intracellular cholesterol metabolism and trafficking
- Expression of lipid transporters
- Cellular pro-inflammatory responses

In vivo studies (rodents)
- Lipidemia and functional serum lipid profile
- Inflammatory markers
- Atherosclerotic lesions

Clinical studies
- Serum cholesterol efflux capacity
- Serum cholesterol loading capacity

PROTEIN HUB



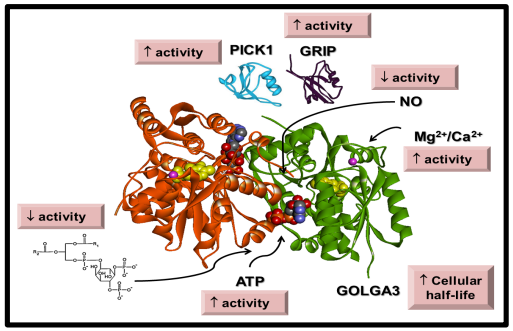
Bruno Stefano (Associate Professor)
Campanini Barbara (Associate Professor)
Mozzarelli Andrea (Professor)

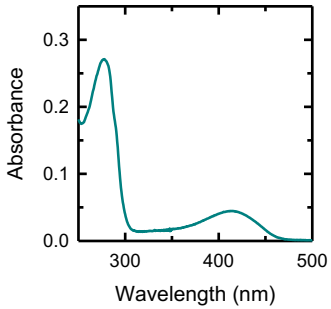
<u>Postdocs</u>
Faggiano Serena
Margiotta Marilena
Paredi Gianluca
Raboni Samanta

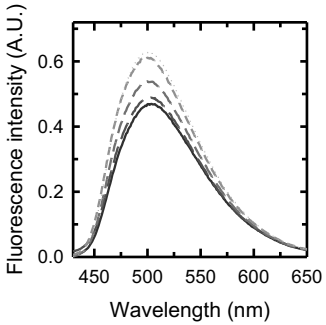
Protein Expression, Purification and Characterization of structure, dynamics, function and regulation

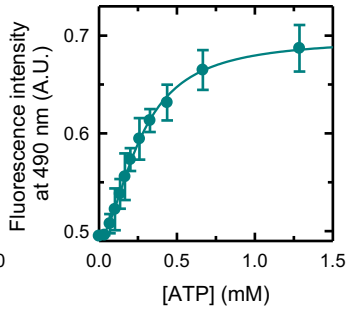
- ***PLP-dependent enzymes*** ⇒ ***serine racemase - target for neuropathologies***
  ⇒ ***O-acetylserine sulfhydrylase – target for adjuvant of antibiotics***
  ⇒ ***methionine gamma lyase – biologics for cancer***

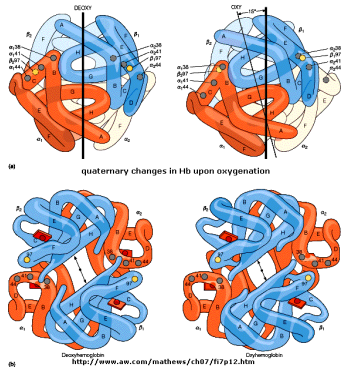
- ***Other enzymes*** ⇒ ***serine acetyltransferase –target for adjuvant of antibiotics***
  ⇒ ***glyceraldehyde-3-phosphate dehydrogenase – target for malaria and cancer***
- ***Other proteins*** ⇒ ***alpha-1-antitrypsin – biologics for pulmonary diseases***
  ⇒ ***Hemoglobins and pegylated hemoglobin – biologics for oxygenation therapy***





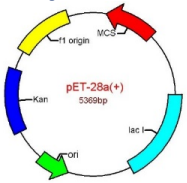






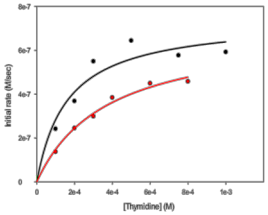
Methods and Instrumentation

Protein engineering and production



Fermentor

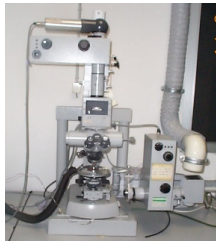
Enzyme assay development, determination of inhibition mechanisms and K_i, rapid scanning stopped-flow

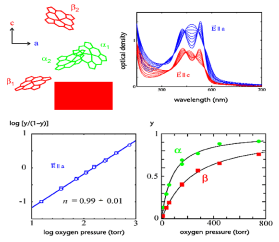


Inhibition profile

Stopped-flow

Spectroscopy and ligand binding of protein in single crystals and encapsulated in silica gels

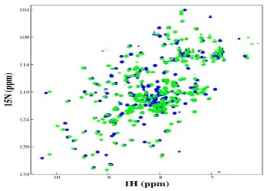




Microspectrophotometer

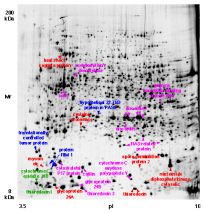
Protein chemical modification

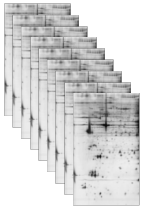
Protein NMR, STD-NMR

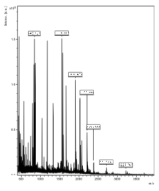


Jeol 600 MHz

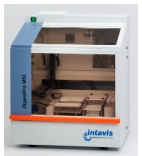
Gel-free and gel-based Proteomics







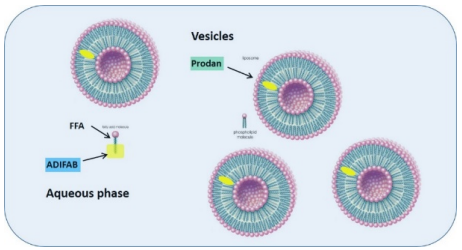
Gel spot cutter

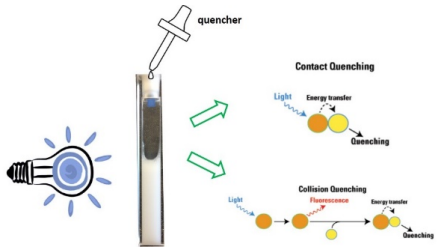


Protein digestor

Mass spectrometer
MALDI TOF-TOF

Structure and stability of formulation by fluorescent solvatochromic probes





The city

PARMA!
City of Gastronomy