

The scientific activity of Linda Celeste Montemiglio is focused on the structural and functional characterization of proteins involved in biological processes crucial for the development of **cancer** and of proteins involved in the **biosynthesis of antibiotics** endowed with potential biotechnological applications. The goal of her research is defining the **biomolecular profile of potential drug target or drug maker proteins**, to understand how they function and control specific aspects of prokaryotic and eukaryotic cells, using a multidisciplinary approach encompassing Molecular Biology, Biochemistry, Biophysics, Structural Biology and Bioinformatics.

The main research lines are focused on:

- **Structural/functional characterization of protein kinase HIPK2 involved in cell development and apoptosis**; she contributed to obtain novel structural/functional insight on a specific posttranslational modification that controls the dual-specific activity of the kinase through biochemical and biophysical methods;

- **Structural/functional characterization of bacterial cytochrome P450s**; the specific expertise of L.C. Montemiglio allowed to reveal a never experimentally demonstrated existence for a P450 of a conformational selection mechanism for substrate binding of the bacterial P450 EryK. Thanks to X-ray crystallographic analysis in conjunction with rapid kinetics and spectroscopic studies, a novel mechanism of substrate binding has been proposed and demonstrated. By means of protein engineering she was able to convert the wild type form of P450 EryK in a high-performing cytochrome able to work on an industrial shunt product of erythromycin (patent). She also determined the 3D structure of a bacterial P450 epoxidase, OleP, in complex with substrate and inhibitor unveiling conformational changes induced by substrate binding and structural/functional features suitable for biotechnological applications.

- **Structural/functional characterization of ferritins (Ft)**; she contributed to define the structural feature of engineered forms of Ft, a humanized *Archeoglobus fulgidus* Ft and a human Ft fused to a lanthanide binding tag by single-particle Cryo-EM measurements. The resulting chimeras are endowed with outstanding nanotechnological properties suitable for application in the field of cancer targeted therapy and biomedicine.

She also determined the structure of the complex formed between the human Ft and the human Transferrin receptor 1 by single-particle cryo-EM (manuscript in preparation).

- **Structural/functional characterization of membrane proteins**; she is working on the determination of the structure and on defining the physiological role of the five isoforms of the SRD5 α (5 α -steroid reductase) membrane-embedded enzymes, major drug targets in the therapeutic field of prostate cancer, preventive field of benign prostatic hypertrophy and therapies for male pattern baldness acne and hormone replacement therapy. Her studies are relevant to rationally design compound able to selectively inhibit the specific isoform, thus reducing or abolishing the debilitating side-effects characteristics of the currently used drugs.