

**PhD position open in the lab of Prof. Cosima T Baldari, Department of Life Sciences, University of Siena, Italy**

*Characterization of the cytotoxic activity of natural and engineered SMAPS in chronic lymphocytic leukemia*

SMAPs (SupraMolecular Attack Particles) are multimolecular complexes with cytotoxic activity recently characterized as the third mechanism of infected or tumoral cell killing by cytotoxic T lymphocytes. While endowed of a core consisting of granzymes and perforin, similar to classical lytic granules, SMAPs are not enclosed by a lipid membrane but by a glycoprotein shell of which a fundamental component is thrombospondin-1 (TSP-1). Since TSP-1 interacts both with ubiquitously expressed receptors and with components of the extracellular matrix, the specificity of SMAPs is limited, however in the physiological context their directional release into the immune synapse ensures a highly selective killing of the target cell. The objective of this project is to make SMAPs exploitable as recombinant cell-free cytotoxic particles. To this aim the mechanisms through which SMAPs interact with target cells will be characterized. Based on this information SMAPs will be engineered to limit their non-specific adhesion while grafting into their shell molecular determinants for the specific recognition of neoplastic cells from chronic lymphocytic leukemia patients. The project will be carried out in collaboration with the partners of the ERC ATTACK project.

The study requires ample and documented knowledge of the cellular and molecular biology of T lymphocytes, especially of the mechanisms that control lytic granule biogenesis and transport. It requires moreover ample expertise in the techniques of molecular and cellular biology, biochemistry and immunology. Finally, it requires strong motivation, ability to work independently, good communication skills and an excellent knowledge of the English language.

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Link for application:

<https://www.unisi.it/didattica/post-laurea/dottorati-ricerca/scienze-della-vita-life-sciences>

Deadline: July 19, 2021