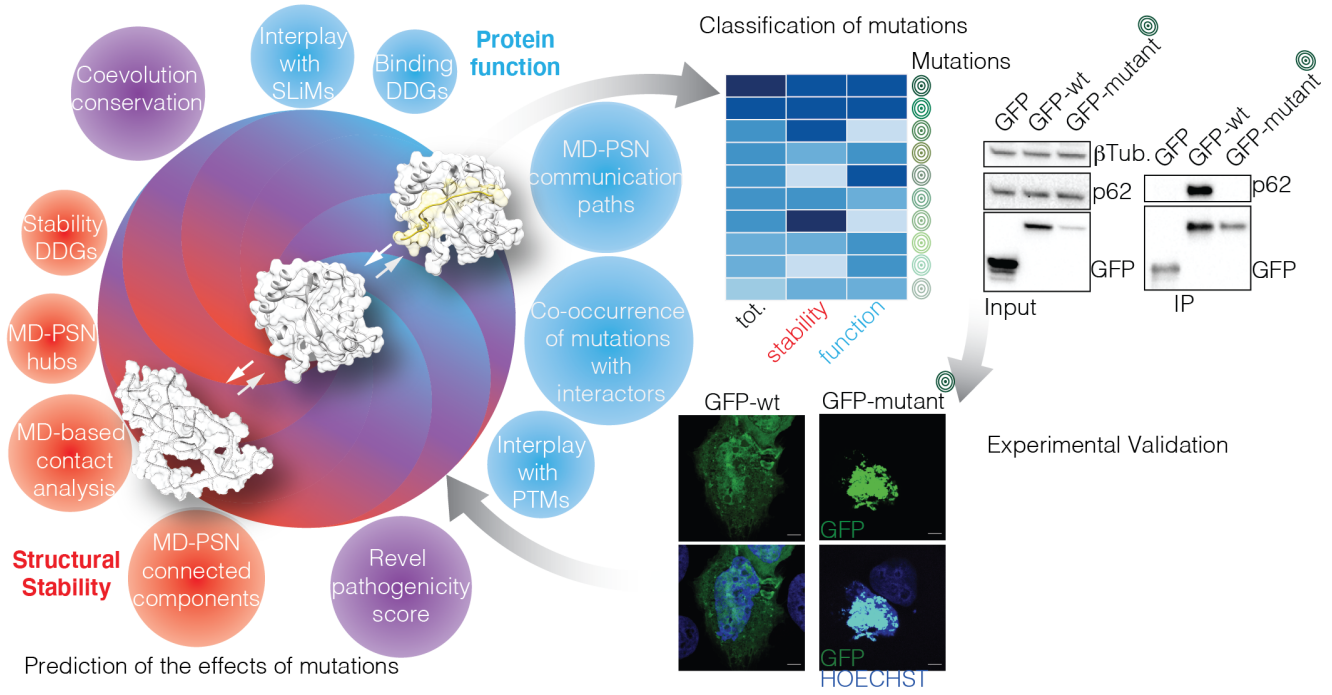
**Annual highlight**

*The conformational and mutational landscape of the ubiquitin-like marker for autophagosome formation in cancer*

-Fas BA et al. *Autophagy* 2020,

Cancer is a heterogeneous group of diseases that originate from the accumulation of harmful genetic alterations. While different cancer hallmarks have been identified cancer heterogeneity and resistance to treatment still stand as important challenges. Uncovering driver alterations and their role in cancer, along with protein candidates for targeted therapy, are open challenges.
Several -omics initiatives have been launched, providing a multitude of quantitative data on different biomolecules characterizing cancer samples. The community needs tools to dissect the complexity hidden in this massive amount of cancer data. In this pilot study, we developed the prototype of an experimentally validated framework integrating structural and -omics analysis for the classification of the impact of mutations found in cancer samples, focusing on a key core autophagy protein, LC3B. We gathered patient cancer mutations of LC3B and characterized them *in silico* for: i) protein stability and misfolding propensity; ii) interaction with biological partners; iii) allosteric behaviour; iv) abolishment of regulation by post-translational modification. The mutations were then scored and ranked to identify the most likely pathogenic variants. As validation, we performed assays based on measurements of protein levels, co-immunoprecipitation, and tendency to form aggregates. Through this approach we found that the LC3B cancer-associated mutation P32Q dramatically impacts on the protein stability and on LC3B interaction with SQSTM1/p62. This first pilot allowed to design and develop a robust workflow, which can be used in a high-throughput manner to screen a larger number of target proteins of interest in cancer.




The figure above illustrates our framework which explores genomics, sequence and structural data (left) and predicts and validates destabilizing mutations for stability or function (right).