



# Systems Pharmacology to personalize Anticancer Therapies (SYSPHARMA)

## U900 - Bioinformatics, Biostatistics, Epidemiology and Computational Systems. Biology of Cancer

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### Team Overview

The quest for personalized cancer management has fostered the development of new technologies enabling the longitudinal assessment of patient- and tumor-specific features at the molecular, tissue and whole organism scales. The systems pharmacology approaches we develop enable the translation of these multi-type datasets into individualized therapies towards significant patient benefit. We aim to design mathematical and statistical methodologies for the personalization of anticancer drug combinations and timing. The developed mathematical models represent the intracellular networks of proteins involved in drug pharmacokinetics-pharmacodynamics (PK-PD), DNA damage response, cell proliferation and cell death, which constitute a reliable physiological basis for the prediction of drug toxicity. Both heterogeneous cancer and healthy tissues are dynamically represented to account for tumour plasticity and tolerability constraints. Physiological rhythms over the 24h span are further included as a major domain of host-tumor differences since normal tissues usually display a robust circadian organization that may be disrupted in tumors. Such detailed mechanistic models are interfaced with statistical algorithms to identify biomarkers to stratify patients and to design patient-tailored multi-agent pharmacotherapies. Because this complex molecular physiology and its temporal organization are unlikely to be completely assessed directly in individual cancer patients, we design multi-scale methodologies integrating in vitro, pre-clinical and clinical investigations in close collaborations with biologists, pharmacologists, oncologists and surgeons.