COLOSYS

Title A systems approach to preventing drug resistance in colon cancer.

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Project partners

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Abstract: Colon cancer (CC) is a major cause of death, and although there are multiple treatments available, not all patients respond in a durable way to a given therapy. It is therefore important to find tumour characteristics that reliable predict whether that tumour will respond to a given treatment. In order to find these characteristics we need to better understand how biomolecules within cells interact with each other in molecular 'networks' that collective control the processes in that cell. In cancer cells these processes behave abnormally due to, for example, mutations that cause the proteins to escape normal control. In order to predict how a cancer cell will react to treatment we need to understand how these networks are structured and how they operate. In the COLOSYS project (www.colosys.org) we will develop a deeper understanding of colon cancer networks and convert them into computer models with

which we will be better capable to predict response to treatment. We will do this, by first gathering data on colon tumours that have been collected in international efforts and use these data to find genes that show frequent abnormal behaviour in colon cancer. Such genes are believed to be 'driving' the disease, they play an important role in response to therapy and most importantly, these genes will help us to focus on the most important parts of the colon molecular network. Next, we will gather all published knowledge on molecular networks in colon cancer in an open repository of data and knowledge, and we will combine this knowledge with the driver genes to construct computer models of the molecular networks in colon cancer. We will then refine these models with data collected on colon cancer cell lines (tumour cells grown in the laboratory), use the models to predict response to therapy and test these predictions on cell lines, on cultures derived from patients (organoids) and on tumours that have been transplanted in mice. The combination of computational, experimental and clinical testing will provide understanding of drug resistance mechanisms, and allow personalised treatment of colon cancer.

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