Factors controlling the order of mutations in colorectal cancer

# Background

As tissues ages, cells accrue mutations. Whilst some mutations lead to cancer, the healthy aged tissue is known to be heavily mutated, and many cancer-associated mutations do not appear to change tissue morphology. It has been proposed that the ordering of mutations may also determine cancer, and in colorectal cancer specific gene interactions have been proposed that may lead to this outcome. In this project you will develop a model of colorectal cancer progression, seeking to explore how gene interactions may explain the apparent importance of orders of mutations.

# Suggested aims

* Build a network consisting of the four key genes and important downstream effectors, and cancer phenotypes. You may wish to draw from the literature (the review includes a simple network) and information in the atlas of cancer signalling networks
* Construct a specification representing the impact of individual and combinations of mutations. Where order of mutations is important, the specification should include all end states (i.e. all orders), and should be tested using LTL (e.g. mutant X and eventually mutant Y implies phenotype Z). Be careful to test all possible endpoints.
* Test and refine the models against the specification, until either fundamental problems in the specification are found or model is correct
* Consider how to expand the model further.

## Relevant resources

<https://biomodelanalyzer.org/>

<https://acsn.curie.fr/ACSN2/ACSN2.html>

## Relevant literature

Review “Molecular interactions in the Vogelstein model of colorectal carcinoma”

<https://pubmed.ncbi.nlm.nih.gov/10699988/>

<https://onlinelibrary.wiley.com/doi/10.1002/(SICI)1096-9896(200003)190:4%3C412::AID-PATH533%3E3.0.CO;2-P>