Contribution ID: **52** Type: **Oral Presentation**

Heritable tumour cell division rate heterogeneity induces clonal dominance

Tuesday, 10 July 2018 12:00 (30 minutes)

Tumours consist of a hierarchical population of cells that differ in their phenotype and genotype. This hierarchical organization of cells means that a few clones (i.e., cells and several generations of offspring) are abundant while most are rare, which is called clonal dominance. Such dominance also occurred in published *in vitro* iterated growth and passage experiments with tumour cells in which genetic barcodes were used for lineage tracing. A potential source for such heterogeneity is that dominant clones derive from cancer stem cells with an unlimited self-renewal capacity. Furthermore, ongoing evolution and selection within the growing population may also induce clonal dominance. To understand how clonal dominance developed in the iterated growth and passage experiments, we built three computational models that simulate these experiments. In the first two models we used the tau-leaping Gillespie algorithm to simulate random growth and passage and we either consider all cells to have an equal proliferation capacity (model 1) or we distinguish between cancer stem cells and differentiated cells (model 2). In the last model, we used a dynamic Monte Carlo method to simulate the development of a cell population where division rates are heritable and vary in between cells due to initial variation and mutation (model 3). Only simulations with the model where division rates varied between the cells (model 3) reproduced the clonal dominance that developed in *in vitro* iterated growth and passage experiments. In contrast, the experimental results can neither be reproduced with a model that considers random growth and passage (model 1), nor with a model based on cancer stem cells (model 2). Altogether, our model suggests that *in vitro* clonal dominance develops due to selection of fast-dividing clones.

Primary authors: Dr PALM, Margriet M. (Division of Drug Discovery and Safety, Leiden Academic Center for Drug Research, Leiden University, The Netherlands); Dr ELEMENAS, Marjet (Division of Drug Discovery and Safety, Leiden Academic Center for Drug Research, Leiden University, The Netherlands); Dr BELTMAN, Joost B. (Division of Drug Discovery and Safety, Leiden Academic Center for Drug Research, Leiden University, The Netherlands)

Presenter: Dr PALM, Margriet M. (Division of Drug Discovery and Safety, Leiden Academic Center for Drug Research, Leiden University, The Netherlands)

Session Classification: The cancer ecosystem: optimizing treatment based on evolution

Track Classification: Evolutionary biology and Genetics