Development of new cell genetic tracing tools for the study of intratumour heterogeneity

Intratumour heterogeneity has been observed in multiple cancers and has been postulated as a critical aspect for tumour metastasis and treatment resistance. Therefore, a further characterization of its role in cancer progression and metastasis has become essential to increase our understanding of cancer biology and to improve the treatment of cancer patients. The use of cell lineage tracing systems, combined with the use of genetically modified mouse models, could be applied in this context. Several genetic tracing systems, based in a random CRE-mediated recombination event in an allele with multiple fluorescent markers surrounded by incompatible lox sites have been created. Once this recombination occurs, the cell and its genetic descendants are permanently labelled with the same fluorescent marker. Nevertheless, these systems present several limitations like a reduced number of potential colour combinations or problems in the unique identification of the markers. Here we have identified new incompatible lox sites that, together with an efficient selection of fluorescent markers, have allowed us to design a new system that will be able to produce up to 15 different colour combinations that can be uniquely identified by confocal microscopy and FACS. This system will be combined with cancer mouse models to study the role and dynamics of intratumour heterogeneity in cancer progression.