Cellular barcoding

It is elusive whether clonal selection of tumor cells in response to ionizing radiation (IR) is a deterministic or stochastic process. With high resolution clonal barcoding and tracking of over 400.000 HNSCC patient-derived tumor cells the clonal dynamics of tumor cells in response to IR was analyzed. Fractionated IR induced a strong selective pressure for clonal reduction which significantly exceeded uniform clonal survival probabilities indicative for a strong clone-to-clone difference within tumor cell lines. IR induced clonal reduction affected the majority of tumor cells ranging between 96-75% and correlated to the degree of radiation sensitivity. Survival to IR is driven by a deterministic clonal selection of a smaller population which commonly survives radiation, while increased clonogenic capacity is a result of clonal competition of cells which have been selected stochastically. A 2-fold increase in radiation resistance results in a 4-fold ($p<0.05$) higher deterministic clonal selection showing that the ratio of these parameters is amenable to radiation sensitivity which correlates to prognostic biomarkers of HNSCC. Evidence for the existence of a rare subpopulation with an intrinsically radiation resistant phenotype commonly surviving IR was found at a frequency of 0.6-3.3% ($p<0.001$, FDR 3%). With cellular barcoding we introduce a novel functional heterogeneity associated qualitative readout for tracking dynamics of clonogenic survival in response to radiation. This enables the quantification of intrinsically radiation resistant tumor cells from patient samples and reveals the contribution of stochastic and deterministic clonal selection processes in response to IR [1)].

1)
Wursthorn A, Schwager C, Kurth I, Peitzsch C, Herold-Mende C, Debus J, Abdollahi A, Nowrouzi A. High complexity cellular barcoding and clonal tracing reveals stochastic and deterministic parameters of radiation resistance. Int J Cancer. 2021 Oct 27. doi: 10.1002/ijc.33855. Epub ahead of print. PMID: 34706068.