Notching up the resensitization against EGFR TKIs in lung adenocarcinoma harboring EGFR « gatekeeper » mutations

EGFR mutated lung adenocarcinoma patients treated with gefitinib and osimertinib show a therapeutic benefit limited by the appearance of secondary mutations, such as EGFRT790M and EGFRC797S. Importantly, we showed that tyrosine kinase inhibitor resistant tumors, with EGFRT790M and EGFRC797S mutations, were highly responsive to the combined treatment of Notch inhibitors with gefitinib and osimertinib respectively. Therefore, our results offer a proof of concept for an alternative treatment to chemotherapy in lung adenocarcinoma osimertinib treated patients after disease progression. I will present published work but also unpublished work we have with SpringWork Therapeutics, owners of the Notch inhibitor Nirogacestat. Our results in preclinical models should pave the way for a clinical trial in our local hospital ICM at Montpellier.

Biosketch

Antonio Maraver has developed his scientific research in international prestigious Institutes as: CNB (Madrid, Spain), The Scripps Research Institute (San Diego, USA), The Skirball Institute of Biomolecular Medicine, NYU (New York, USA) and CNIO (Madrid, Spain). He has contributed as first or last/corresponding author in: Nature, Cancer Cell, Journal of Clinical Investigation or Blood to name only a few. Since January 2015 he is group leader of the "Oncogenic pathways in lung cancer" laboratory at IRCM (Montpellier, France).