David Santamaría received his PhD from University Autónoma of Madrid (Spain) in 1999, under the guidance of Prof. Jorge B. Schwartzman, studying replication fork barriers. He then joined the laboratory of Prof. Ronald A. Laskey, (1999-2003) at the Wellcome/CRC Institute (Cambridge, UK) where he dealt with the initiation of DNA replication and its connection with cell cycle control. He returned to Spain (2003-2016) as a staff scientist in Prof. Mariano Barbacid group (CNIO, Madrid) where he used mouse genetics to conduct a comprehensive analysis of the Cyclin Dependent Kinase family and to identify therapeutic targets in lung adenocarcinoma. He joined the IECB in 2016 and obtained a DR2 INSERM position starting January 2018.

We use mouse models to characterize new signalling pathways and oncogenic functions that govern the onset of lung adenocarcinoma (LUAD). We have a particular interest in the mechanisms that regulate the initiation, intensity and duration of the RAS-ERK signalling. The regulation of this pathway is an essential feature controlling tumour initiation, disease progression and drug resistance to several targeted agents. Our work in collaboration with Dr Chiara Ambrogio identified a key role of KRAS membrane dimerization/clusterization in this process. Our immediate goal is to understand the molecular basis underlying this feature and to functionally characterize protein factors required to assemble a KRAS-dependent signalling platform on the inner plasma membrane. As a whole, this approach may identify novel therapeutic targets with low toxicity and potential clinical applicability in LUAD.

Recent publications:

1. Sanclemente, M., Nieto, P., Garcia-Alonso, S., Fernández-García, F., Esteban-Burgos, L., Guerra, C., Drosten, M., Caleiras, E., Martinez-Torrecuadrada, J., **Santamaría, D.**, Musteanu, M. and Barbacid, M. (2021) RAF1 kinase activity is dispensable for KRAS/p53 mutant lung tumor progression. ***Cancer Cell***. doi: 10.1016/j.ccell.2021.01.008.

2. Nokin, M.J., Ambrogio, C., Nadal, E. and **Santamaría, D.** (2020) Targeting Infrequent Driver Alterations in Non-Small Cell Lung Cancer. ***Trends Cancer***. doi: 10.1016/j.trecan.2020.11.005.

3. Nokin, M.J., Darbo, E., Travert, C., Drogat, B., Lacouture, A., San José, S., Cabrera, N., Turcq, B., Prouzet-Mauleon, V., Falcone, M., Villanueva, A., Wang, H., Herfs, M., Mosteiro, M., Jänne, P.A., Poujol, J.L., Maraver, A., Barbacid, M., Nadal, E., **Santamaría, D***. and Ambrogio, C*. (2020) Inhibition of DDR1 enhances in-vivo chemosensitivity in KRAS-mutant lung adenocarcinoma. ***JCI Insight*** doi: 10.1172/jci.insight.137869. * Co-corresponding authors.

4. Ambrogio, C., Köhler, J., Zhou, Z., Wang, H., Paranal, R., Li, J., Capelletti, M., Caffarra, C., Li, S., Gondi S., Hunter, J.C., Chiarle, R., **Santamaría, D.**, Westover, K.D. and Jänne, P.A. (2018) KRAS dimerization impairs sensitivity to MEK inhibitors and is essential for oncogenic activity of mutant KRAS. ***Cell*** 172(4), 857-68.e15. doi: 10.1016/j.cell.2017.12.020.

5. Nieto, P., Ambrogio, C., De Esteban, L., Gómez-López, G., Blasco, T., Yao, Z., Marais, R., Rosen, N., Chiarle, R., Pisano, D.G., Barbacid, M. and **Santamaría, D.** (2017) A B-Raf kinase inactive mutant induces lung adenocarcinoma. ***Nature*** 548, 239-43.