



## PhD position for 4 years for biologists or computational scientists to work on cancer evolution

Contract for 4 years enrolled in the PhD programme of the Neuroscience Institute in Alicante, Spain to work in the lab of Prof. M. Angela Nieto, "Cell movements in development and disease" **Available to start next academic year (2025-2026).**

We are seeking a highly motivated candidate to join us on a transversal project. Intratumoral cell heterogeneity is a hallmark of cancer evolution, influencing metastatic potential and patient outcomes. This diversity arises from the accumulation of genetic mutations and genome-independent mechanisms, such as cancer cell phenotypic plasticity, mainly through epithelial-to-mesenchymal transitions (EMT) (Nieto et al., Cell 2016; Mehta and Stanger, Cancer Res. 2024). Recently, we have demonstrated that cancer cells evolve in the tumor by adopting one of two opposing plasticity trajectories: an embryonic-like migratory path that promotes metastasis or an adult-like injury response path that fosters anti-tumour inflammation (Youssef et al., Nature Cancer, 2024). This provides a novel framework to interpret tumour evolution.

We study now not only cancer cells but also their interactions with stromal populations in breast cancer models using single-cell transcriptomics, chromatin structure and computational analysis of cell-cell interactions plus spatial transcriptomics. This allows the description of functional interactions and the associated signalling pathways. Analysing the tumour-stromal interactome from the perspective of cancer cell plasticity offers a transformative approach to understanding breast cancer evolution. This framework holds the *potential to reveal interconnected pro-tumour and anti-tumour responses*, which can help improve patient stratification, and uncover novel targets to guide therapeutic strategies, ultimately aiming at improving clinical outcomes.

### Selected recent references from the lab:

- Gonzalez-Iglesias et al. (2024). Intron detention tightly regulates the stemness/differentiation switch in the adult neurogenic niche. **Nature Comm.** 15, 2837. <https://doi.org/10.1038/s41467-024-47092-z>
- Youssef et al. (2024). Two distinct Epithelial to Mesenchymal Transition Programmes Control Invasion and Inflammation in Segregated Tumour Cell Populations. **Nature Cancer** 5, 1660–1680. <https://doi.org/10.1038/s43018-024-00839-5>
- Youssef and Nieto (2024). The epithelial-mesenchymal transition in tissue repair and degeneration. **Nature Rev Mol Cell Biol.** 25, 720-739. <https://doi.org/10.1038/s41580-024-00733-z>

Interested candidates with good academic record please send a letter of motivation describing the interest in our project together with a CV and two contacts for reference letters.

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