

**AZ funded Non clinical PhD Studentship in “*Therapeutic cancer prevention of hereditary cancers*” (Fixed Term)**

**Project abstract:** Despite major advances in the development of immune and targeted-therapies, the molecular and cellular complexity of late-stage tumours remains a major barrier to treatment. This makes a strong case for focusing on identifying those at risk of developing cancer and intervening prophylactically to prevent tumour development. By identifying early cellular and molecular changes that occur in the tissue, we could develop effective early detection and intervention strategies. Over the last 10 years my lab has used a combination of single cell genomics, mouse models and primary human samples to map cellular changes in the breast during homeostasis and tumour initiation (*Reed, Pensa et al 2024 Nature Gen., Twigger et al 2022 Nat. Comm., Bach, Pensa et al. 2021 Nat. Comm., Bach et al. 2017 Nat. Comm.*). We have mapped the precancerous cellular changes that occur in human *BRCA1* carriers and in a mouse model of *Brca1* and identified several precancerous cellular changes. This in turn opens the possibility to exploit our cellular and molecular understanding of breast tumour initiation for the development of therapeutic prevention strategies. In this project, we will explore the potential use of a couple of drugs developed by AZ in modulating these precancerous changes and preventing tumour development.