A novel Src-FRET biosensor mouse providing real-time insights into the dynamic spatiotemporal regulation of Src activity during cancer progression

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Introduction: Cancer progression, invasion and metastasis depend on the complex interactions between malignant cells and their surrounding environment. Intravital (in vivo) imaging is providing new insights into how cells behave in their native microenvironment in real-time and can serve as a dynamic readout of therapeutic response. The family of Src kinases are a well-known driver of cell proliferation, survival and motility and are commonly overexpressed and hyperactivated during cancer progression, invasion and metastasis. Here, we have generated a Src biosensor mouse based on the well-validated Src-FRET biosensor to visualise the spatiotemporal activity of Src kinase in live tissues in real-time.

Methods and Results: We demonstrate (i) that fluctuations in Src activity can be quantified in any live tissue of interest in physiological and pathological contexts, (ii) that single-cell and subcellular Src activity can be tracked during cancer cell mobilisation and (iii) that our biosensor mouse in combination with titanium optical imaging windows can serve as an in vivo platform from which to rapidly assess the efficacy of anti-invasive therapy.

Conclusions: We suggest that our new Src biosensor mouse can be used (i) as a versatile model to quantify Src activity in a broad range of contexts highlighting the wider applications of our technology, (ii) as a novel tool to fundamentally expand our understanding of cancer spread in vivo in native microenvironments and (iii) as a novel pre-clinical drug-screening platform to predict cancer spread and to estimate the efficacy of anti-invasive treatment in vivo.