Name	ERIK SAHAI
Position	Senior Group Leader Assistant Research Director
Year joined *(Crick or founder institute)*	2004

Career History

PREVIOUS POSITIONS
1998– 2003: Post-doctoral Fellow, Institute of Cancer Research, 237 Fulham Road, London
2003– 2004: Post-doctoral Fellow, Albert Einstein College of Medicine, NY, USA
2004– 2010: Junior Group Leader, CRUK London Research Institute, 44 Lincoln' Inn Fields, London
2010– 2015: Senior Group Leader, CRUK London Research Institute, 44 Lincoln' Inn Fields, London

EDUCATION
1991– 1994: First Class Bachelor's degree in Zoology, University of Cambridge, UK
1994- 1998: PhD in Biochemistry – supervisor Richard Treisman, University College London, UK

Major Awards, Honours and Prizes

1994 University of Cambridge Frank Smart Prize for Zoology
2003 – 2004 UICC Translational Cancer Research Fellowship
2008 EMBO Young Investigator Programme Member
2009 British Society for Cell Biology Hooke Medal
2014 Elected EMBO member
2017 Elected Fellow of the European Academy of Cancer Sciences
2021: Elected Fellow of the Academy of Medical Sciences

Membership of external committees, editorial boards, review panels, SABs etc

REVIEW PANEL ROLES
• CRUK Science Committee (since 2016)
• CRUK/EPSRC Multidisciplinary Project Award Committee (since 2015)

STEERING/ADVISORY COMMITTEES
• Academic Steering Committee for CRUK clinical training accelerator award (since 2017)
• Training Steering Committee for CRUK City of London Major Centre (since 2019)
• National Cancer Research Institute Strategic Advisory Group member (since 2020)

JOURNAL EDITORIAL ROLES
• Editorial board member of Molecular and Cellular Biology (since 2010)
• Editorial board member of Oncogene (2011-2019)
• Editorial board member of Journal of Cell Biology (since 2013)
• Editorial advisory board member of Journal of Cell Science (since 2015)
• Editorial board member of Developmental Cell (2020)
• Editorial board member of Trends in Cell Biology (2020)

OTHER
2020 - President Elect of the Metastasis Research Society

Lab Name	*Tumour Cell Biology Laboratory*

Research programme and achievements

At the beginning of the QQR period, the Sahai group was focused on investigating cancer invasion, including regulation of the actomyosin cytoskeleton, and how cancer-associated fibroblasts (CAFs) and the organisation of the extra-cellular matrix (ECM) modulate the behaviour of cancer cells. This work included discovering heterotypic cell-cell contacts between cancer cells and fibroblasts that mechanically couple the two cell types, documenting how cGAMP transfer at this interface promotes the expression of inflammatory modulators by CAFs, and how collisions between fibroblasts lead to the generation of aligned ECM. In the course of this work, we additionally discovered how CAFs modulate responses to targeted therapies, with the relationship between the tumour microenvironment and therapy responses becoming increasingly prominent in our research. We also found out how epithelial cells in the local environment of indolent micro-metastases provide support to cancer cells.

Current and future work in the group is divided into three interconnected areas: 1) Understanding how cell-cell and cell-ECM interactions spatially pattern the tumour microenvironment 2) Studying how non-genetic inter-cellular heterogeneity in cancer cells affects therapy responses and 3) Defining the rules and mechanisms of clonal competition in established tumours and how these are affected by the cell-cell interactions and spatial features of tumours. We employ an inter-disciplinary approach to tackle these problems with mathematical methods of data analysis and computational modelling becoming prominent. These are linked to both experimental models and analysis of patient tissue. We also use various forms of optical imaging to pursue our research, and work closely with the Photonics Satellite group from Imperial College.

Research outputs

Arwert EN, Milford EL, Rullan A, Derzsi S, Hooper S, Kato T, Mansfield D, Melcher A, Harrington KJ, Sahai E. (2020) ***STING and IRF3 in stromal fibroblasts enable sensing of genomic stress in cancer cells to undermine oncolytic viral therapy*****. Nature Cell Biology (7):758-766. DOI: 10.1038/s41556-020-0527-7**
This work shows why stromal fibroblasts are an important source of inflammatory modulators in tumours. We show fibroblasts can respond to cGAMP produced by cancer cells, but only when the two cell types are in direct contact. This in turn promotes the STING and IRF3 dependent expression of interferon beta and various chemokines. The subsequent up-regulation of interferon-stimulated gene expression undermines the efficacy of oncolytic viruses. We propose the requirement for direct contact represents a 'tissue level' mechanism for triggering this response specifically in the context of tissue damage, as in healthy tissue, the basement membrane precludes such interactions.

Montagner M, Bhome R, Hooper S, Chakravarty P, Qin X, Sufi J, Bhargava A, Ratcliffe CDH, Naito Y, Pocaterra A, Tape CJ and Sahai E. (2020) ***Cross-talk with lung epithelial cells regulates Sfrp2 expression enabling disseminated breast cancer cell latency.*** **Nature Cell Biology (3):289-296. DOI: 10.1038/s41556-020-0474-3**
We set up a complex model for lung alveoli by co-culturing lung fibroblasts and alveolar epithelial type I and type II cells on a gas permeable support, with the expectation that the fibroblasts would strongly influence the behaviour of cancer cells introduced into the system. However, we discovered that the largest effect came from the alveolar epithelial cells, and we then used a range of approaches to delineate the signalling mechanisms involved. This work, together with a concomitant study from the Malanchi group,

established the role of epithelial cells in the tumour microenvironment of indolent and micro-metastases.

Park D, Wershof E, Boeing S, Labernadie A, Jenkins RP, George S, Trepat X, Bates P and Sahai E. (2020) *Extracellular matrix anisotropy is determined by TFAP2C-dependent regulation of cell collisions.* Nature Materials 19, 227-238. DOI: 10.1038/s41563-019-0504-3
In this study, we used our bank of patient-dervied stromal fibroblasts to ask why some fibroblasts generate highly aligned extra-cellular matrices and other do not. We were able to show how cell migration and cell-cell collisions can dictate the patterns formed by fibroblasts, and that furthermore, the higher order organisation of fibroblasts and matrix is associated with millimetre scale contraction of reconstituted tissues and cancer invasion. The quantitative tool developed during the course of this work and a related study is now being tested for its prognostic value in simple histological stains of breast and prostate cancers.

Ege N, Dowbaj AM, Jiang M, Howell M, Jenkins RP*, Sahai E*. (2018) *Quantitative Analysis Reveals that Actin and Src-family kinases regulate nuclear YAP1 and its export*. Cell Systems 6(6):692-708. DOI: 10.1016/j.cels.2018.05.006
We previously demonstrated that YAP1 is critically required for the activation of stromal fibroblasts. In this paper, we showed that contrary to received wisdom, YAP1 is not stably sequestered when inactive, and its sub-cellular distribution is largely regulated at the level of nuclear export. Subsequently, Rob Jenkins (SLRS in Sahai group and co-corresponding author) has established a collaboration with the Mathematics department at the University of Nottingham to further develop the quantitative basis of this work, including the derivation of chromatin binding on and off rates from simple photobleaching experiments.

Labernadie A, Kato T, Brugués A, Serra-Picamal X, Derzsi S, Arwert E, Weston A, González-Tarragó V, Elosegui-Artola A, Alcaraz J, Roca-Cusachs P, Sahai E*, Trepat X*. (2017) *A mechanically active heterotypic E-cadherin/N-cadherin adhesion enables fibroblasts to drive cancer cell invasion.* Nature Cell Biology 19(3):224-237. DOI: 10.1038/ncb3478
Our previous work showed how stromal fibroblasts lead the collective invasion of cancer cells, and documented how remodelling of the extracellular matrix was important for this behaviour. Following our observation of direct cell-cell contacts between cancer cells and fibroblasts, we hypothesised that the two cells might be mechanically coupled; therefore, we began collaborating with Xavi Trepat (IBEC Barcelona), who is a world leader in the mechanics of multi-cellular systems. By biophysical measurements and a range of conventional cell and molecular biology manipulations, we demonstrated that fibroblasts actively ‘pull’ cancer cells into the surrounding extracellular matrix.