ECM regulation of metastasis

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Metastasis is responsible for over 90% of cancer patient deaths, and is a process strongly regulated by the extracellular matrix (ECM). Studies have shown that the ECM can promote or restrict cancer progression, and that targeting cell-ECM interactions at the primary tumour can disrupt tumour growth and invasion as well as improve drug response.

We developed a method called In Situ Decellularisation of Tissues (ISDoT) to isolate structurally intact 3D ECM organ scaffolds from healthy and tumour-bearing tissue. This has enabled us to study the metastatic niche in great detail, and map ECM proteins to the metastatic niche for further characterisation. We have used the information gained to target cell-ECM interactions at the metastatic niche, which has disrupted metastatic growth in each instance.

We then developed the ISDoT method to use the ECM scaffolds as a bioreactor to culture cells, and have been able to model metastatic colonisation and outgrowth. We are now investigating how cancer cells respond to healthy versus metastatic ECM. We further developed the ISDoT method to enable decellularisation of human tissue to isolate 3D intact ECM scaffolds. Though artifical intelligence machine-learning analysis of immunostaining images, we compared ECM of healthy versus diseased lungs and uncovered new features of disease.

More recently, we have explored the role of ECM stiffness on metastatic outgrowth of cancer cell subpopulations. We identified sub-populations of cancer cells with differential responses to ECM and validated key pathways involved in promoting or suppressing metastatic cancer cell outgrowth.

Our results show the power of the ECM in harnessing or promoting cancer metastasis. We aim to translate our findings into the clinic to help patient lives.