Combinatorial effects of matrix stiffness and ECM proteins on cell behaviour and morphology

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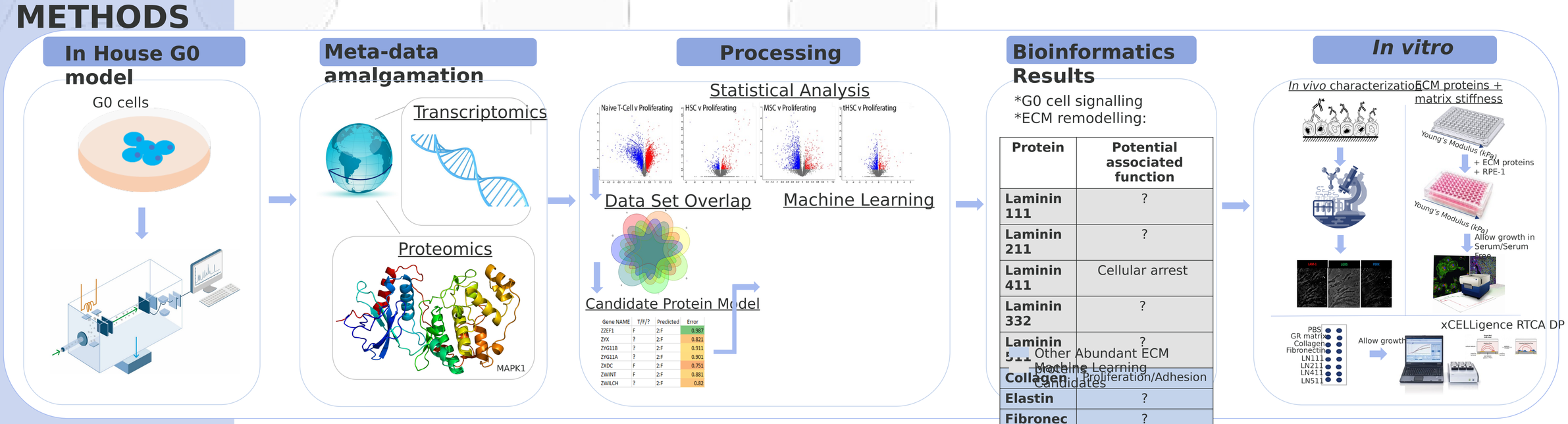
INTRODUCTION

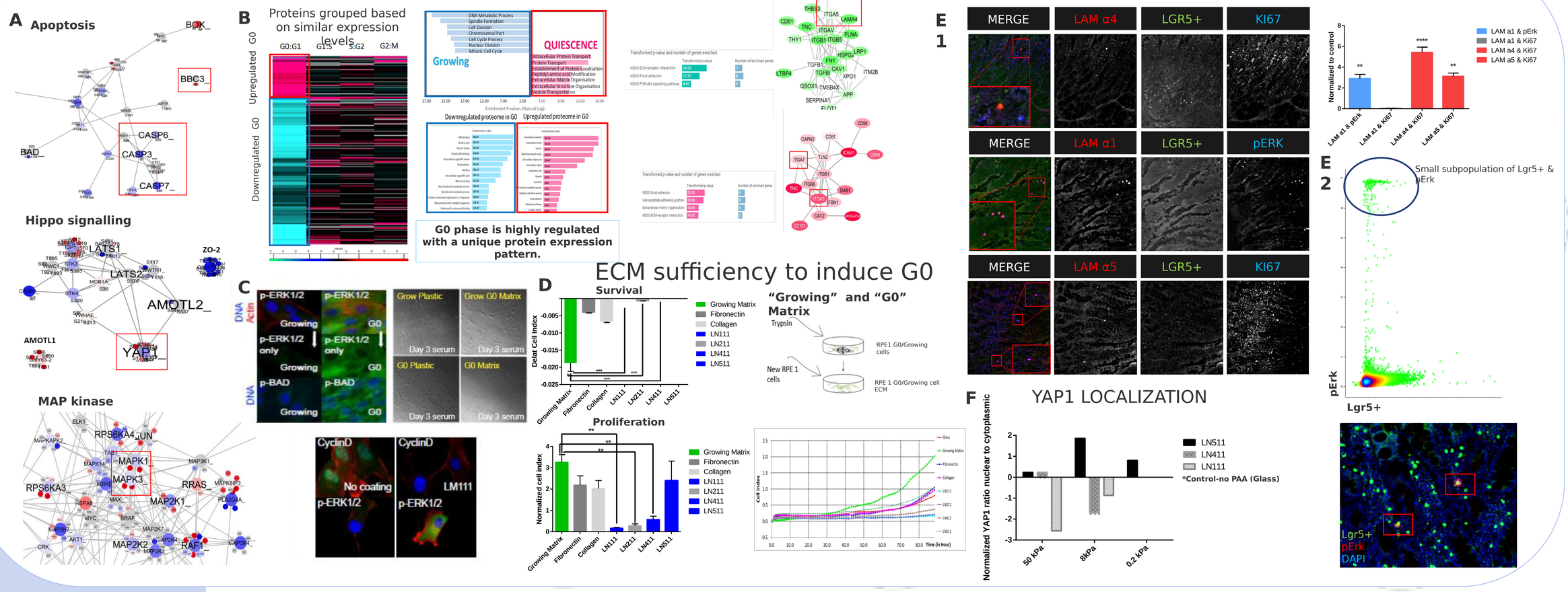
Stiffness of a matrix (resistance to deformation), is one of the many mechanical forces acting on cells and is increasingly appreciated as an important moderator of cell behaviour. It broadly regulates cell signalling, with major effects on growth, survival and motility. Particularly, the Hippo and YAP/TAZ signalling pathways have been identified as a major mechanical sensing signalling arms within the cell. Although, the effects of stiffness for different adherent cell types vary, generally, cell proliferation and differentiation increase with the stiffness of the matrix. This study explores the collaborative effect of matrix stiffness and various types of ECM proteins on cell behaviour and YAP/TAZ signalling.

METHODS



RESULTS

G0 signalling



CONCLUSIONS &

- Subset of laminin coated matrices can induce characteristics associated with quiescence (G0).
- G0 cells have a unique modulation MAP kinase signalling cascades.
- In isolation laminins:111 and 411 do not support cellular growth, while in the presence of growing cell matrix and laminin 511, cells grow rapidly.
- *In vivo* laminin α1 was discovered to colocalize with stem cells that have a G0 signature, while laminin α4 and α5 colocalize with proliferating cells.
- At higher matrix stiffens supplemented with laminin 511 YAP1 is nuclear, while at the same stiffness but in the presence of laminin 411 and 111 YAP1 is cytosolic.