



# Manipulating cell-microenvironment interactions by inducing rapid integrin endocytosis in Ovarian Cancer

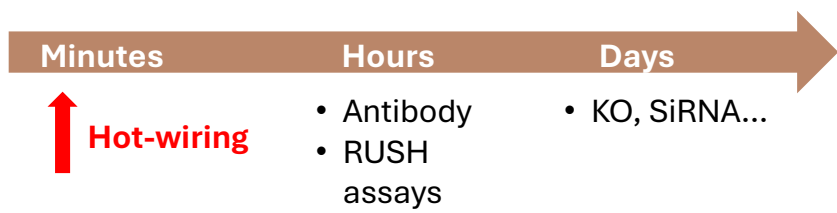


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## Background

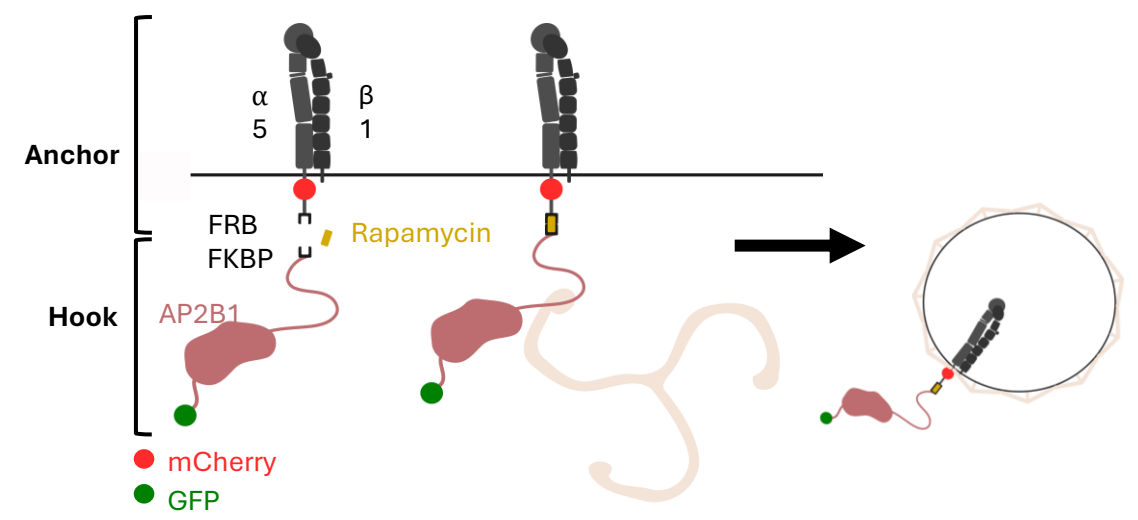
The way that cells “talk” to their microenvironment is dependent on the number of integrins at their surface. Being able to modulate integrin availability at the surface would allow us to modulate cell-cell and cell-microenvironment interactions and understand how these interactions impact cell behaviour. In the context of ovarian cancer,  $\alpha 5\beta 1$  and  $\alpha v\beta 3$  integrins are especially interesting, 1)  $\alpha 5\beta 1$  is implicated in every step of ovarian cancer dissemination, 2) there is a reciprocal crosstalk between  $\alpha 5\beta 1$  and  $\alpha v\beta 3$ , 3) both bind fibronectin as a ligand. How can integrins be modulated?



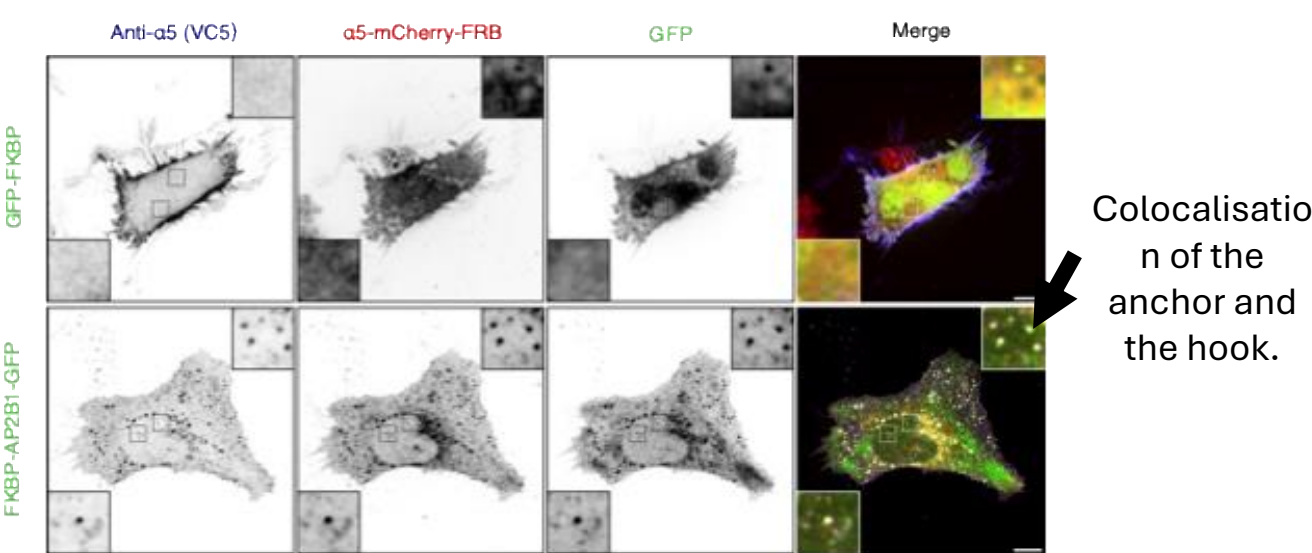
**Goal:** Rapidly remove  $\alpha 5\beta 1$  or  $\alpha v\beta 3$  from the cell surface to modulate cell behaviour.

Hot-wiring method was designed in our lab to rapidly remove CD8 from the cell surface by clathrin-mediated endocytosis<sup>1</sup>.

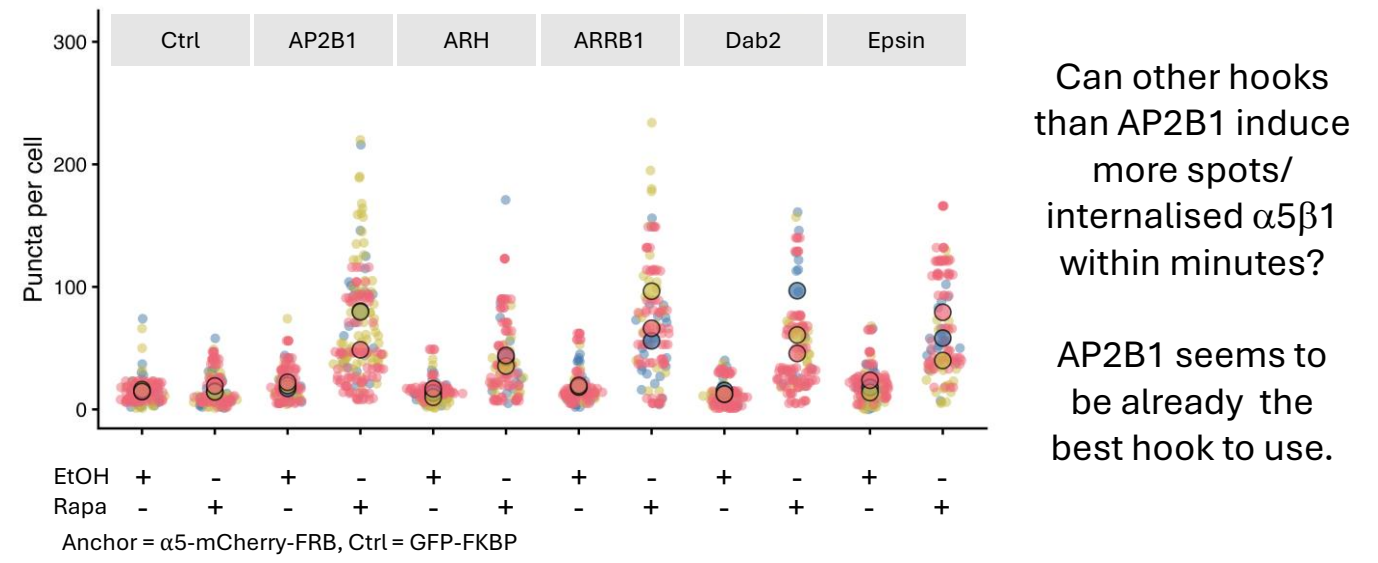
### Hot-wiring: $\alpha 5\beta 1$ endocytosis through clathrin pathway



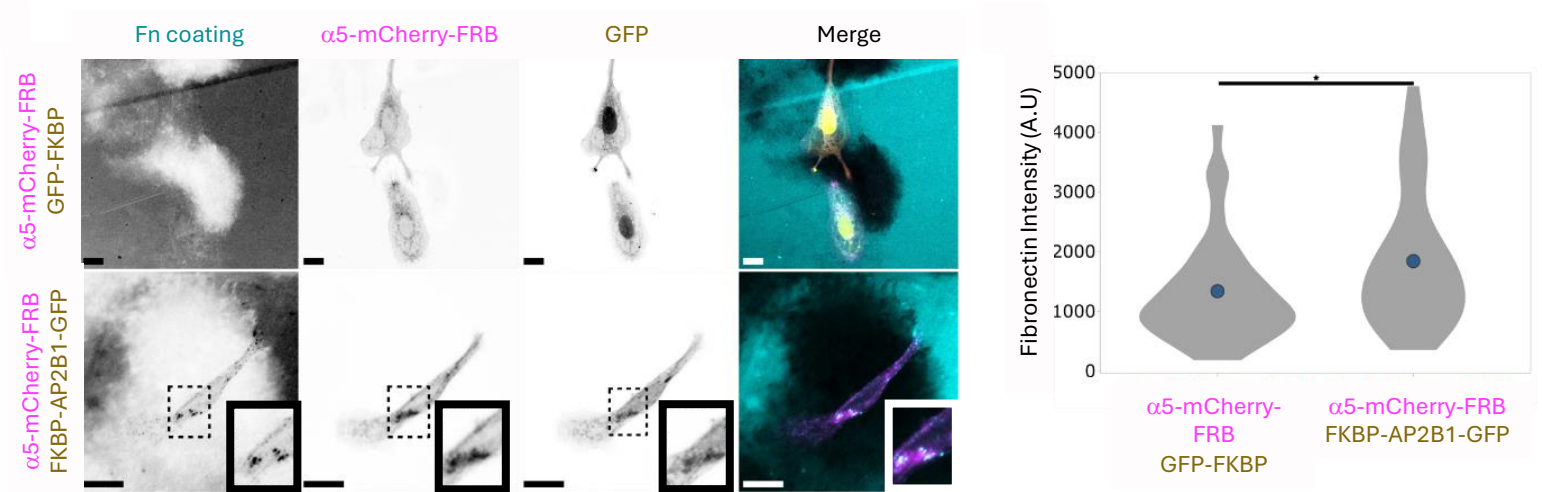
## 1 $\alpha 5$ and $\beta 1$ are internalised with Hot-wiring



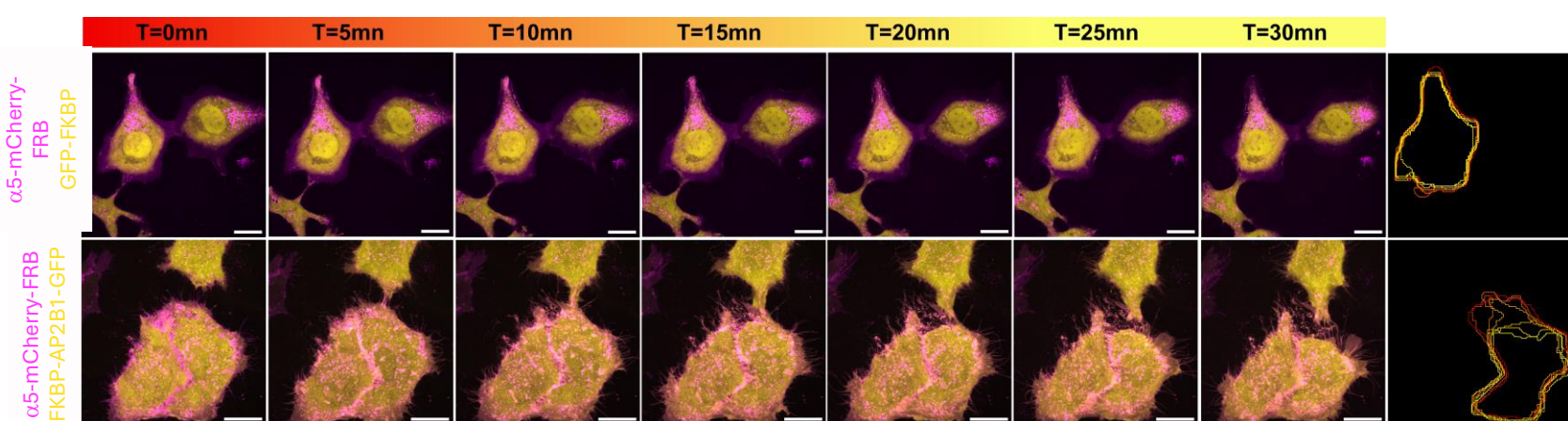
## 2 Optimising $\alpha 5\beta 1$ endocytosis



## 3 Induced internalisation of integrin $\alpha 5\beta 1$ causes fibronectin uptake



## 4 Hot-wiring of $\alpha 5\beta 1$ induce cell retraction

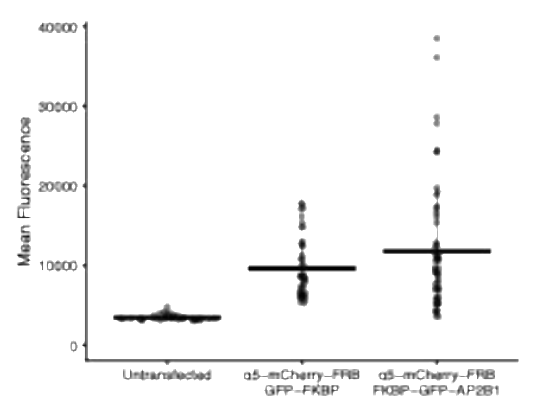


Endocytosis of  $\alpha 5\beta 1$  within minutes, in SKOV3 cells, induce change in cell phenotypes.

### Next steps

- Currently working on tagging all endogenous  $\alpha 5$  or  $\beta 3$  in SKOV3 cells (ovarian cancer cell line) by CRISPR.
- Study the effect of modulating  $\alpha 5\beta 1$  and  $\alpha v\beta 3$  on cell-cell and cell-microenvironment interactions (3D complex models).

## 5 Next steps



Transient transfection is used to express the hot-wiring system. Tagging integrins by CRISPR knock-in should give clearer phenotypes.