# CELLULAR DECISION-MAKING DURING CANCER

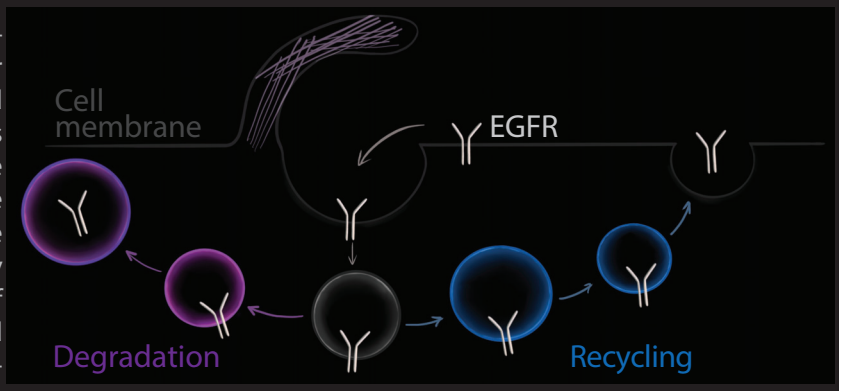
UNSW SYDNEY

EMBL Australia

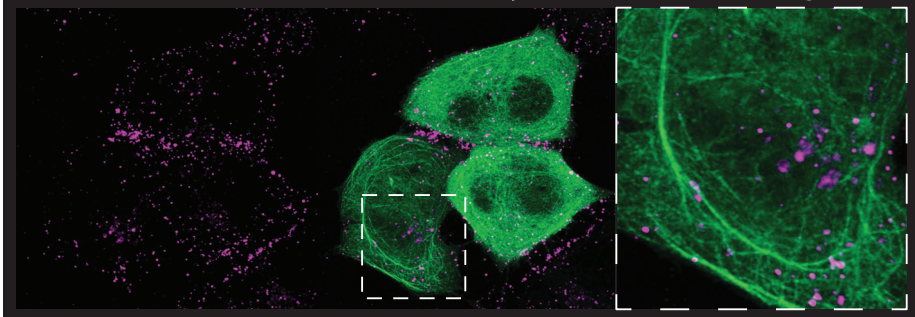
## Cytoskeleton and Motors Lab @ Single Molecule Science

### Problem: EGFR and cancer

In a large percentage of lung and breast cancers, signalling through the epidermal growth factor receptor (EGFR) is increased, promoting cell proliferation and migration central to cancer development. Multiple drugs for treating these cancers (e.g. Gefitinib, Erlotinib) induce EGFR endocytosis, or uptake, removing EGFR from the plasma membrane and terminating signalling. These drugs are highly effective, but all patients eventually develop resistance to them. A better understanding of how EGFR levels at the plasma membrane are controlled is required for the development of effective, resistance-proof cancer treatments.



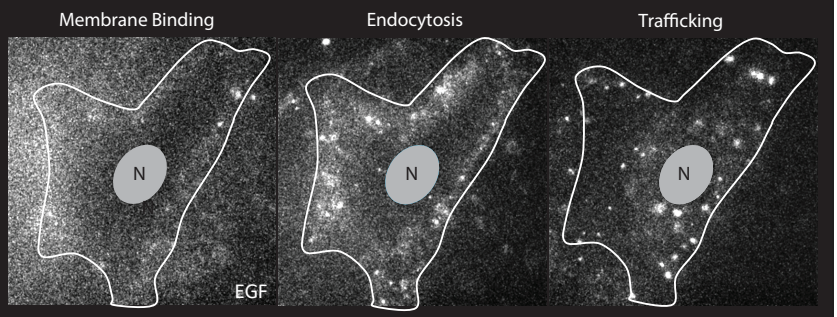

### Approach I: Super-resolution analysis of EGFP coupling to microtubules



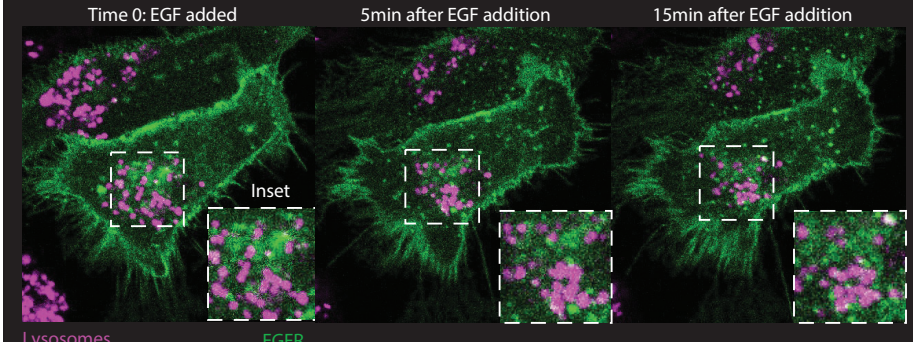

If EGFR is recycled, more signalling occurs- a bad prognosis for cancer. If EGFR is degraded, signalling is terminated. The cellular decision making determining if EGFR is recycled or degraded is not well understood. Using super-resolution imaging, we will dissect how molecular motors couple EGFR to microtubules, the highways within the cell that deliver receptors for recycling or degradation.

### Approach II: Rapid, live-cell EGFR tracking

With rapid live cell imaging, we can track every aspect of EGFR endocytosis and trafficking, imaging single endosomes from the moment they appear though to their final destination. Using two EGFR ligands: epidermal growth factor (EGF) and transforming growth factor α (TGFα), we can determine the molecular switch controlling the balance between EGFR degradation and recycling.




### Approach III: Imaging the intracellular fate of EGFR




Ultimately, we want to understand EGFR trafficking so we can target it for degradation. By coupling live-cell imaging with addition of EGFR ligands and drugs that manipulate EGFR fate, we will uncover a comprehensive map of EGFR trafficking. This project will ultimately open new avenues for anti-cancer therapeutics that overcome the development of resistance to current EGFR drugs.


### Contact us!

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