**Cell polarity**

With the advent of advanced microscopy techniques, particularly fluorescence microscopy which allowed the localisation of specific proteins to be probed in cells, patterns began to be observed on an intracellular scale

**The Min system**

MinD promotes its own membrane association (how?) and recruits MinE (following a delay). MinE negatively regulates the membrane binding of the MinDE complex, leading to dissociation into the cytoplasm and break-up of the complex. The result is formation and rapid disassembly of a domain on the membrane. This oscillates from pole to pole (why?)

The result is that time averaged Min(C?) concentration is lowest at the cell centre. As Mins negatively regulate Z-ring assembly, this results in Z-ring assembly, and therefore cytokinesis, taking place at the cell centre.

This system has been successfully reconstituted in vivo, giving rise to a variety of behaviours characteristic of Turing-like mechanisms such as <> (Zieske and Schwille 2014)

**CDC-42 polarity in yeast**

Yeast cells use cdc-42 polarity to direct an asymmetric cell division (/budding)

Positive feedback locally amplifies Cdc42 concentrations. Membrane bound CDC42-GTP recruits Bem1, which recruits cdc42 (need to brush up on details).

Long-range inhibition is provided via depletion of a limiting cytoplasmic pool. Growth of the cdc42 domain reduces this pool, which stalls growth.

**PAR polarity**

A final example of cell polarity is PAR polarity. Best studied in the developing C elegans embryo, PAR polarity plays an essential role in development by regulating a series of asymmetric cell division. PAR proteins form patterns on the cell membrane which direct asymmetric localisation off the spindle and asymmetric distribution of fate determinants. The resulting cell division is asymmetric, leading to two cells that differ in size and fate.

The PAR network is a highly conserved network of proteins that drives polarity in a range of cell types across the animal kingdom (Goldstein and Macara, 2007). PAR polarity plays a number of essential roles throughout development, including asymmetric cell division, cell fate specification, regulation of tissue architecture and cell motility. Key to this process is the formation of asymmetric PAR protein patterns at the cortex of cells. PAR polarity is distinct from the two other examples described so far as it relies on two distinct groups of proteins, referred to as anterior and posterior PARs (aPARs and pPARs) that show distinct and complementary cortical patterns. Rather than self-amplification, in which one protein (or group of proteins) directly feeds back onto its own local enrichment, the dominant patterning mechanism in PAR polarity is one of mutual antagonism, whereby proteins within the two subgroups negatively regulate each-other’s localisation (Goehring).

A classic model system for studies of the PAR network is the C. elegans zygote. PAR proteins were first found to be important for this process in a screen of mutants that disrupt asymmetric zygote divisions (Kemphues and others… Tabuse, Watts). Work in the following decades has gone to characterize the PAR proteins as a diverse and highly conserved set of scaffold proteins, adaptors and enzymes, some which play essential roles in the self-organisation of PAR polarity (Lang). Key to this process is cross-phosphorylation of the two subgroups, driven by kinases within each group, which negatively regulates membrane association and keeps the domains separate (refs).

Once PAR polarity is set up, enzymes within each group direct a set of downstream processes, leading to asymmetric segregation of cell fate determinants (Cuenca, 2003; Daniels et al., 2010; Griffin et al., 2011; Wu et al., 2018) and asymmetric placement of the cleavage plane (Bouvrais et al., 2018). The net result is an asymmetric cell division, with daughter cells differing in both size and fate. This process repeats in subsequent cell divisions, playing an essential role in early patterning of the embryo. FIGURE

As well as the C elegans embryo, PAR protein homologies display asymmetric localization in many different organisms and cell types, where they play a number of essential roles. <More needed here, e.g. neuroblasts. Mechanisms may differ, such as unipolar polarity without an opposing domain in some cases>.

*Epithelia*

See Rodriguez-Boulan review

PAR proteins play a key role in organising apical-basal polarity in epithelia

Essential for their selective barrier and transporter functions

The arrangement and roles of this polarity depends on the tissue.

Actin-rich microvilli form a brush border on the apical surface of intestinal cells

A junctional region forms between the apical and basolateral domains, which provides cell-cell adhesion and barrier functions.

As well as the PAR proteins, there are a number of other players that are more specific to epithelia (CRB, SCRB)

Clusters of PAR-3 appear at the cortex, and are transported towards the future apical surface, carrying PAR-6/PKC-3, and helping to organise junctional proteins (Pickett, others). This doesn’t appear to be driven by the actin cortex (ref? see Pickett discussion), but may rely on microtubules instead.

Basolateral proteins, such as LGL <> which are known targets of PKC-3, are cleared from the apical surface. In contrast to the zygote, however, removal of PAR-3 or PKC-3 does not appear sufficient to block this clearance, indicating that other mechanisms may play a role (Pickett 2021, check also Mike Boxem’s stuff)

*Neuroblasts*