TOPIC 1: TISSUE ORGANISATION AND TISSUE DYNAMICS

Tissue dynamics

(utilizes multiple cell fate processes – cell replication, differentiation, cell death, migration, adhesion)

Tissue homeostasis

- natural growth and regeneration of cells - maintain equlibrium
- facilitated by adult stem cells within that environment
- different tissues have different regenerative capacity

Tissue repair (eg wound healing)

- Multiple stages; requires a lot of signaling to get cells to right location at right time
    - Homeostasis and inflammation stage
        - macrophage, neutrophils kill bacteria and clean wound
        - chemotactic agents recruit other cell types to wound - eg fibrobasts
        - Fibroblasts form ECM
        - Keratinocytes release other signals to recruit cytokines and GFs
        - Endothelial cells repair blood vessel
    - Proliferation stage
        - Fibroblasts and keratinocyte proliferate to produce more skin
            - Fibroblasts release cytokines (interleukin 1) & GFs to cause keratinocytes to proliferate
    - Remodelling stage
        - Synthesis and degradation of collage and other ECM materials
        - Balance between factors that promote ECM formation & enzymes that breakdown ECM
        - Cell migration

Tissue formation (morphogenesis)

- TE aims to repair tissue that cannot be repaired by intrinsic repair mechanism → therefore have to replicate organ formation during embryogenesis
    - Consider - Origin of cells, GFs, differentiation, organ formation, interaction between cells and environment
    - Normal development - gastrultion (3 germ layer formation though cell interaction, cell movement, morphogen signaling, gradients of TGFB growth factors and BMP4)
    - Neural crest cells display extreme plasticity and is a good cell source for TE
    - Eg bone formation

TOPIC 2: CELL FATE PROCESSES & CELL SIGNALLING

Cell fate processes – proliferation, differentiation, migration death, attachment

<u>Cell replication/proliferation</u>

○ If growth is unconstrained:

$$\frac{dX}{dt} = \mu X$$

$$X(t) = X_0 e^{\mu t}$$

Where
$X(t)$ = number of cells at a given time
μ = growth rate
t_d = cell doubling time
~ 12 – 30 h for human cells in culture

- If constrained by media available (michaelis-menten)

○ Constrained growth can be approximated by:

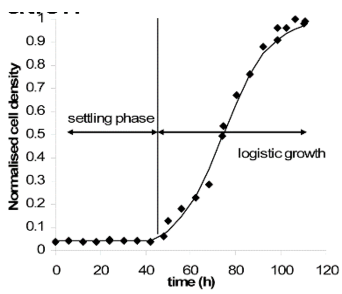
$$\mu([C]) = \frac{\mu_{Max}[C]}{K_m + [C]}$$

Where
μ_{Max} = maximum achievable growth rate
[C] = concentration of limiting component
K_m = concentration at which half maximal growth is achieved

- If constrained by space (eg monolayer formation, log growth)

Logistic Growth: $$\frac{d\langle u\rangle}{dt} = \alpha\langle u\rangle(1-\langle u\rangle)$$

$\langle u\rangle$ = normalised mean cell density
α = cell growth rate
= 0.097 h^{-1} (fibroblasts on TCP)



<u>Cell differentiation</u>

- Measured by changes in gene expression, cell function/features, and mathematical model

$$\frac{\partial X}{\partial t} + \delta(a)\frac{\partial X}{\partial a} = 0$$

<u>Cell death</u>

- Can be death by apoptosis (natural homeostasis) or necrosis (induced)
- Natural apoptosis:

$$\frac{\partial X}{\partial t} = \alpha X$$

$$\alpha([C]) = \frac{\alpha_{Max}\cdot[C]}{K_m + [C]}$$