

LECTURE 2 – INNATE IMMUNE MECHANISMS

- **Innate and adaptive systems**
 - Operate in parallel and interact in both health and disease
 - Innate systems influence adaptive responses
 - Can prime the adaptive system and amplify levels of activity
 - Innate system is **rapid** (seconds, minutes, hours)
 - Adaptive system is **delayed** (days, weeks) and **protracted** (weeks, months, lifelong)
 - Each system can be viewed as protecting the host but protection is dependent on context
 - Same systems activated at the wrong time in wrong place and for the wrong duration may harm the host

LECTURE 3 – ADAPTIVE IMMUNE MECHANISMS

- **Principle: specificity** to foreign antigens; **tolerance** to self
- Key cells in the adaptive immune system:
 - **Antigen presenting cells** (e.g. dendritic cells); **lymphocytes** (T cells – CD4+ helpers, CD8+ cytotoxic; B cells – antibodies)
 - CD = **clusters of differentiation** (antigens expressed on T cell surface which help to identify the differentiation of the cell)
- **Endotoxin** (lipopolysaccharide) – fragment of gram negative bacterial cell wall – binds CD14 and TLR4 – trigger rapid (hours) production of IL-1 alpha, TNF alpha and chemokines
 - Also **reinforces adaptive immune system** by inducing **co-stimulatory molecules** on antigen presenting cells → enables adaptive immunity (antigen-specific T and B cells)

LECTURE 5 – GLUCOCORTICOIDS

- **Roles**
 - **Physiological roles** – e.g. replacing cortisol in individuals who are deficient to allow for usual physiological roles to occur
 - **Pharmacological roles** – e.g. anti-inflammatory, immunosuppressant, anti-cancer
 - Doses of steroid in excess of physiological amount
- **Cortisol** “stress hormone”
 - Synthesised by the adrenal cortex
 - Affects carbohydrate and protein metabolism – essential for life
 - Cortisol has **glucocorticoid** activity – anti-inflammatory (at supraphysiological level) – and **mineralocorticoid** (influence salt and water balance) activity
 - I.e. cortisol can bind to each of these distinct receptors with similar potency, to promote different actions
 - Synthetic corticoids tend to have greater glucocorticoid (anti-inflammatory) potency

LECTURE 12 – SMOOTH MUSCLE in the RESPIRATORY SYSTEM

- **Lung airway architecture**
- Number of airways doubles at each airway branch
- 23 generations of **bifurcations**
 - Increasing number of parallel units moving down the bronchial tree
 - Generation 0 = trachea
 - Generation 1 = 2 main bronchi
 - Generations 2-4 = large bronchi
 - Generations 5-11 = small bronchi
 - Generation 12- 23 = bronchioles
 - Number of airways = 2^g (g = generation)

LECTURE 13 – DRUGS IN ASTHMA

- **Definition of asthma**
- A chronic inflammatory disorder of the airways
- Chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing
- Widespread, variable and often reversible (spontaneous/with treatment) airflow limitation
- Many cells and cellular elements play a role

LECTURE 16 – DRUGS TO TREAT CANCER 1

- Therapeutic objectives
- **Primary prevention**
 - E.g. smoking cessation, Coxibs (polyps – not yet a tumour but can develop into one)
- **Elimination of tumour cells (cure)**
 - May require a combination of approaches
 - Surgical resection of solid tumour
 - Organ specific radiotherapy (breast)
 - Cycles of chemotherapy
 - Targeted therapy – small molecules and biologicals
 - Immunotherapy
 - Cell therapy (e.g. transgenic cells, autografts)
 - Most attempts at cure are thwarted by the development of resistance

LECTURE 21 – DRUGS TO TREAT HYPERTENSION

- **β 1-adrenoceptor antagonists**
- Contribute to decreasing in blood pressure by influencing:
 - HR, SV, contractility, preload, venous tone, intravascular volume, $\text{Na}^+/\text{H}_2\text{O}$ retention
- β 1-adrenoceptor stimulation supports cardiac performance
 - β agonists increase β 1-adrenoceptor mediated increases in Ca^{2+} during systole
 - Increased Ca^{2+} entry increases fractional shortening of cardiac muscle during contraction