Ask Weber

Topic 18/19

Energy and metabolic pathways

Topic 19

Microbiome

THE UNIVERSITY OF SYDNEY

Microbes on our body

What is the difference between a pathogen/parasite and a commensal?

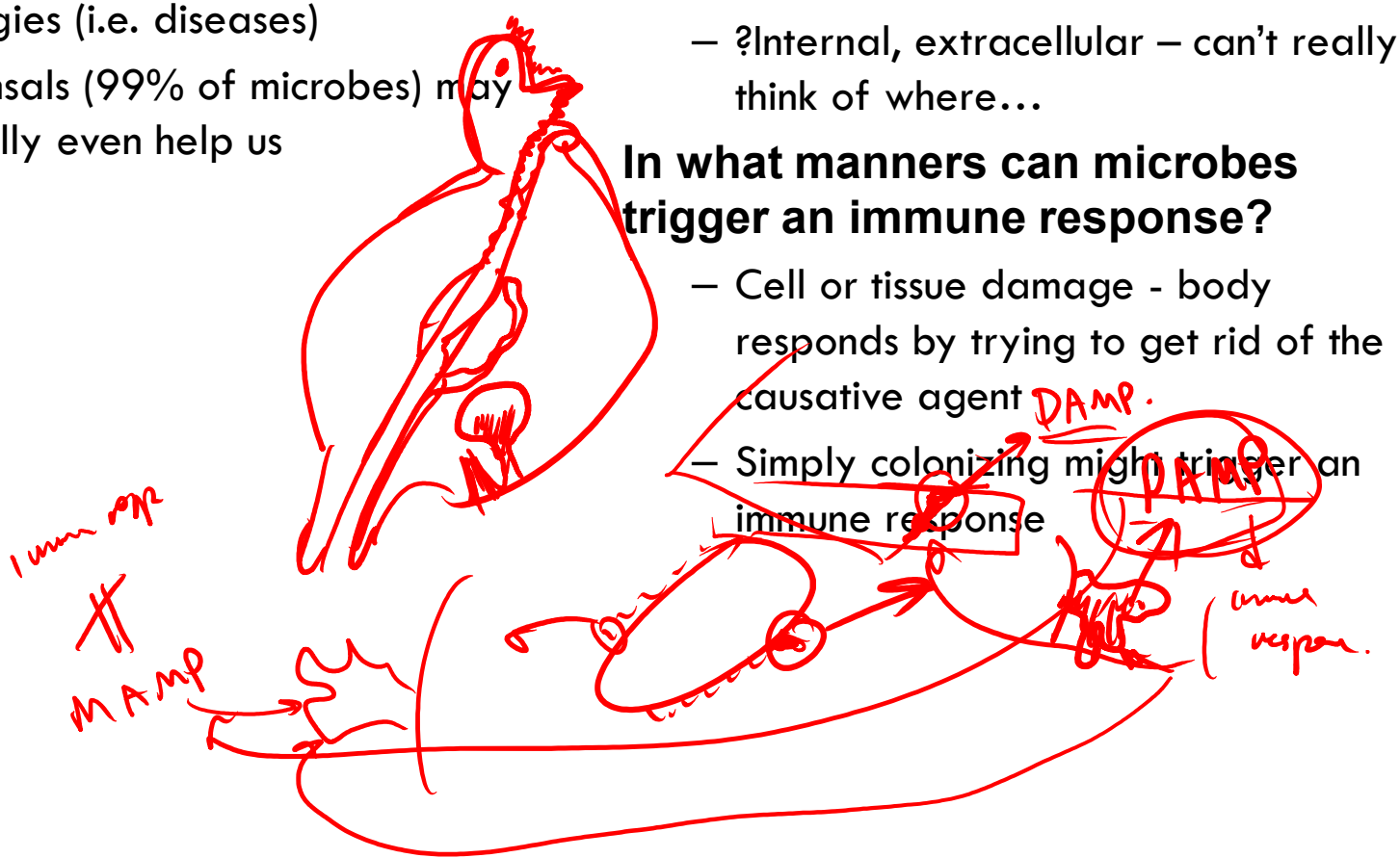
- Pathogens and parasite can cause pathologies (i.e. diseases)
- Commensals (99% of microbes) may potentially even help us

Where on the human body do microbes typically colonise?

- Skin
- Gut, oral mucosa, etc
- ?Internal, extracellular – can't really think of where…

In what manners can microbes trigger an immune response?

- Cell or tissue damage - body responds by trying to get rid of the causative agent
- Simply colonizing might trigger an immune response



Immune responses

What are the 2 main types of immune responses and what do they do?

- Innate immunity – a general immune response that initiates inflammation and attacks anything foreign
  - Might also induce programmed cell death for identified infected cells
- Adaptive immunity – a specific immune response to a target organism/microbe, can produce specific antibodies

How does a strong immune response potentially hurt us?

- Ongoing damage can occur
- Inflammation might kill the bacteria/microbe, but inflammation is NOT good for us (think of this – chronic inflammation is considered a precursor to cancer)
  - Chronic inflammation will result in tissue damage
- Immune complex formation – antibodies can form clumps and deposit in random places where we don't want them to (e.g. HenochSchonlein purpura, an IgA vasculitis)
- Autoantibody formation (e.g. rheumatic fever after a Group-A Streptococcus infection – can cause endocarditis, higher risk in Indigenous children)
- Cell death, inflammation, etc.

DAMP, MAMP, PAMP

What is the function of a DAMP, and what is the function of a PAMP in the case of an organism such as Vibrio cholerae?

- Vibrio cholerae is a pathogen. All pathogens will activate an innate and adaptive response. DAMP and PAMPs are part of the innate response
  - DAMP – Damage associated molecular patterns; essentially any molecules which are found on HUMAN CELLS WHICH ARE DAMAGED
  - PAMP – Pathogen associated molecular patterns (which is now called MAMP – microbe associated molecular pattern) are molecules which are found on MICROBES

What do MAMPS, DAMPS do?

- The body's immune cells will recognize MAMPs and DAMPs
- Just note that DAMPs should not really be present in the normal, healthy human – MAMPs might be (as not all microbes are bad), but they shouldn't really be in the blood…
- These cells in the innate immune system respond by activating inflammation, etc.

The microbiome

How do microbes affect our gut function postnatally?

Does the large or the small intestine have more microbes?

- Large intestine has more

Difference between small and large intestine microbiome? What about in herbivores vs carnivores?

- SI – stable occupation by distinct microbes
  - Microbes in herbivores allow for fermentation in herbivores, but tends not to be as common in carnivores
- LI – higher density

Microbiome in the large intestine

What are the most common microbes in the gut?

- Bacteria most common
  - Bacteroidetes – involved in fermentation and breakdown of large chain polysaccharides into short chain fatty acids
  - Firmicuties – fermentative metabolism
  - Proteobacteria – metabolically diverse, fermentation, more commonly break down sugars, amino acids, small chain fatty acids
- Archaea
  - Methanobrevibacter- involved in methanogenesis, breakdown of small carbons into methane!

How do intestinal microbes allow us to maximise carbohydrate consumption in vegetables?

- Large intestine microbes secrete enzymes, ferment sugars and synthesize biomolecules
- They allow slow transit of 'fibre', in the process breaking down insoluble polysaccharides (e.g. cellulose – in plant walls) and exposing nutrients within cells that can then be altered and absorbed (incl. SCFA, amino acids, vitamins, etc.)

Microbiome benefits to us

What short chain fatty acids are produced by the microbiome in the large intestine?

- Via fermentation, simple carbohydrates can be converted into
  - Acetate
  - Propionate
  - Butyrate
  - Etc

What is the function of butyrate in our gut?

- Butyrate acts as an energy source for the colon – It is produced BY bacteria in the colon, FOR the colon!

How can a gut microbiome dysregulation result in formation of a toxic metabolite?

- Sulfate reduction can occur, which converts short chain fatty acids into H2S (rotten egg gas) via an anaerobic respiratory process

Microbiome benefits to us

What is nutrient control?

- Control of nutrients available to different segments of the digestive tract
  - Small intestine has all nutrients absorbed quickly, quick passage means limited time to grow
  - Large intestine works much slower, creates a different nutritional milieu
- Fermentative metabolism in large colon allows release of SCFA and fibre metabolism
  - Low iron = low oxygen = anaerobic/fermentative respiration
  - Nitrogenous wastes (urea, uric acid) allows growth on fibre