Main introduction

1. HCMV and HHV

1.1. Herpesviridae: humanity's long-term viral companions.

quick recap of diseases and burden of HCMV and HHV

Long evolution of HHV, traces present in neanderthal dna evem

OScars paper etc – a lot of diversity, a lot is linked to MHC subclasses hence the immunological interplay

Linked to complex conditions like MS, cancers, sporadic conditions outlining

Target the immunologically weaker populations

1.2. Epidemiological picture of HCMV burden

Newborns, need for vaccine (more deets about that later). Epidemiology, incidence etc etc etc, SEP connection. Hygeine hypothesis ?

Bring the epi brain to this section

1.3. HCMV: molcularly complex pathogen

1.3.1 Virion structure

1.3.2 Establishing life-long latency in the host

1.3.3 Epigenetic changes

Only infects a certain lineage. Contribution to haematopoiesis

1.3.4. Glycorprotein repertoir of HCMV virion

– describe the function of all

1.3.5. Entry and tropism

– so nmany receptors for all. Nectin, heparin etc etc. Placenta transmission?

Crucially – when compared to HHV its similar but some bits are missing. Spend a few days writing this.

1.4. Glycoprotein B as a universal fusogenic machine

- gB in. the context of other fusion proteins. review that Matt sent to me and Al, about fusion proteins in general + influenza haemoglutennin being a loaded spring. Compare all side by side – can they all be the loaded spring ? Mechanistical function in fusion

1.5. HCMV gB immunogenicity

Antigenic domain galore.

All ADs, how often they induce reponse naturally etc

1. Vaccine strategies

2.1 HHV vaccines

Only VZV – and thats attenuated. Look at the diversity between VZV and others – is that the reason? Or the relatively mild clinical picture

2.2 HCMV vaccines

A review of all vaccines – many many many papers

2.3 gB-based vaccines

Stopping gb means stopping fusion means stopping infection

Other gB vaccines ?

GB/MF59 as the pinnacle – go through all clinical trials like the undergrad diss

2.4 Mechanism of protection

- neutralising and non neutralising responces in HCMV vaccines etc

1. Research questions of this manuscript

Summarise briefly

Analsyis of gB. Can we understand more about HCMV and HHV biology and life cycle? Can we make a better HCMV gB vaccine?

Abstract for each chapter? Would be cute.