VIRAL IMMUNOLOGY

Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens

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Background

- Measles endemic in much of the world → >100,000 deaths yearly
- Increase in M&M for as long as 5 years after infection
- Since 2018 increased incidence as a result of reduced vaccination
- Importance of understanding consequences of measles virus infection
- Immunosuppression after measles:
  - 1908 Clemens von Pirquet: negative cutaneous tuberculin reaction in children
  - Decreased interferon signaling, skewed cytokine response, lymphopenia
  - MV receptor highly expressed on memory T, B, Plasma cells → «Immunological amnesia»
- **Aim:** identify and quantify effects of measles on the immune system
Methods

• Paired blood samples from unimmunized children during a measles outbreak in the Netherlands
  ➢ children who developed measles (n=77)
  ➢ uninfected children (n=5)

• Control cohorts
  ➢ age-matched controls, sampled 3 months apart (n=28)
  ➢ age-matched controls, sampled 1 year apart (n=31)
  ➢ adult controls (n=22)
  ➢ children before and after MMR vaccination (n=33)

  o Mild measles (n=34)
  o Severe measles (n=43)
## Methods

- VirScan: PhIP-Seq technology
Methods

• Expanded VirScan Library
  ➢ Full proteomes of most viruses
  ➢ Many bacterial proteins

• Comprehensive measure of antibody repertoire diversity

• Epitope binding signal (EBS): a relative measure of antibody titer for each epitope
Results and discussion
Antibody repertoire diversity

Cntl A: age-matched, 3 months
Cntl B: age-matched, 1 year
Cntl C: healthy adults
Antibody repertoire diversity

- Mean reduction of 20% in the overall diversity or size of the antibody repertoire after MV infection
- Increase in MV-specific epitopes in children after measles or MMR vaccination
- No changes in total IgG (ELISA)
- Restructuring of the antibody repertoire after measles
Effect on preexisting immune memory

- Controls retained 90% of their repertoires

- After severe or mild measles, children lost a median of 40% or 33% respectively, of their total preexisting pathogen-specific antibody repertoires
Effect on strength of epitope recognition

After measles 40% reductions in EBSs
Effect of MMR vaccine on immune repertoire
Reconstruction of the immune repertoire

• Subset of children with increased EBS for specific pathogens after measles → New exposure?

• High transmissible respiratory pathogens

• Spatially clustered?
Reconstruction of the immune repertoire
Experimental measles infections

- 4 rhesus macaques
- VirScan antibody profiling before and 5 months after measles
- Each monkey lost, on average, 40 to 60% of its preexisting antibody repertoire
Conclusions

• Measles is associated with large reductions in both the diversity of the antibody repertoire and magnitude of the binding signal

• Rebuilding of immune memory through reexposure → increased clinical risks

• Measles vaccine does not impair immune repertoire, on the contrary, prevents immune amnesia and reduces morbidity and mortality risks