

What shapes the human immune system?

Michelle Linterman

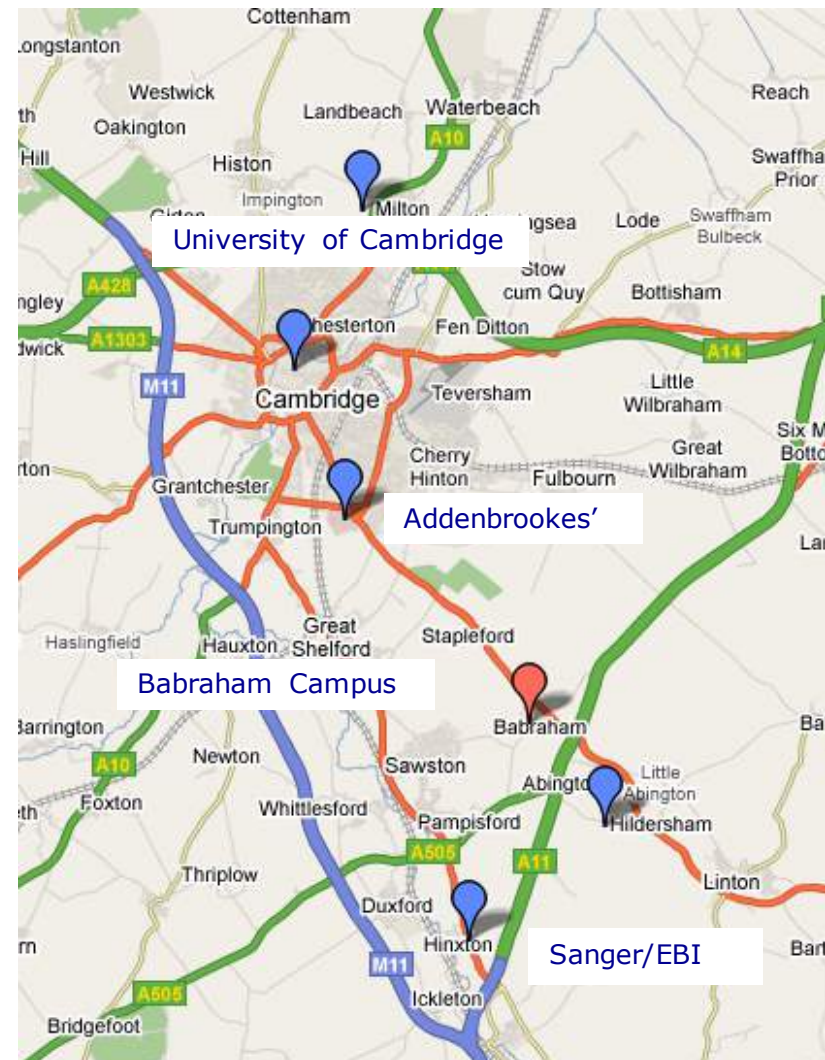
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 @LintermanLab

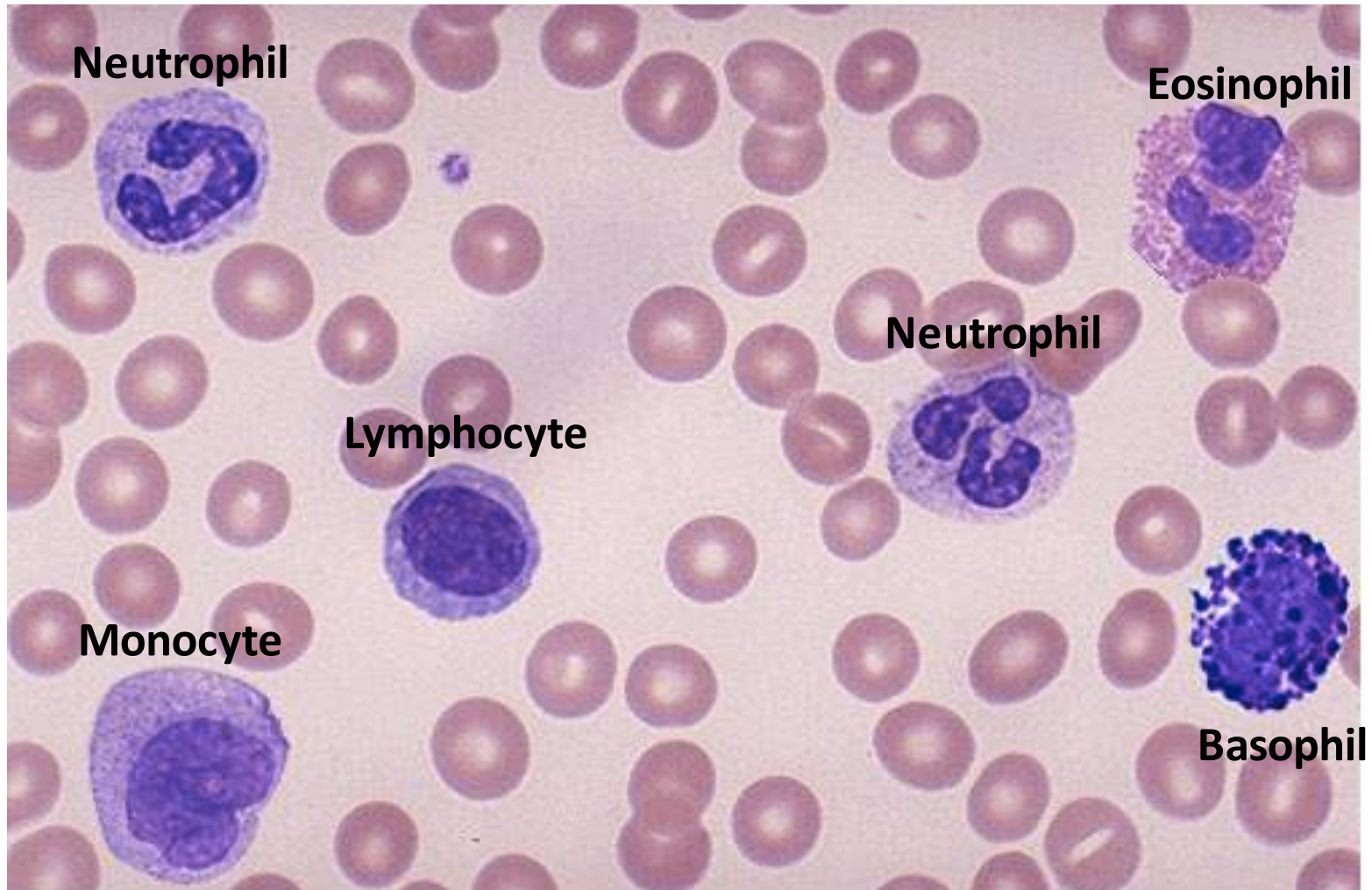


Babraham Institute

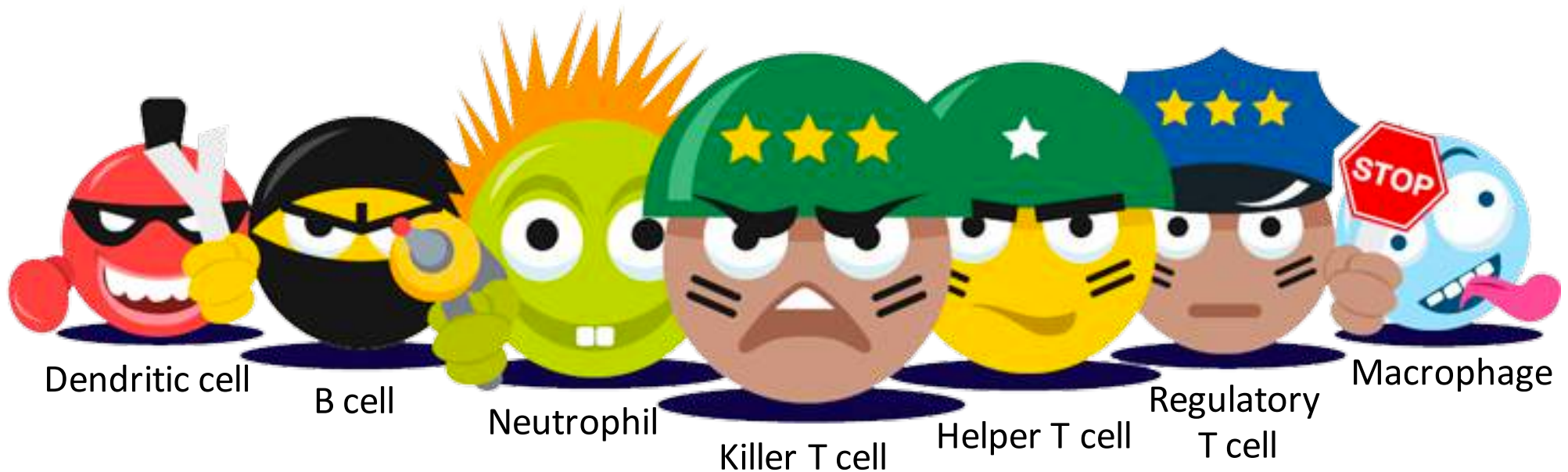
- BI: An independent research Institute sponsored by the BBSRC.
- Research focuses on basic bioscience underpinning health



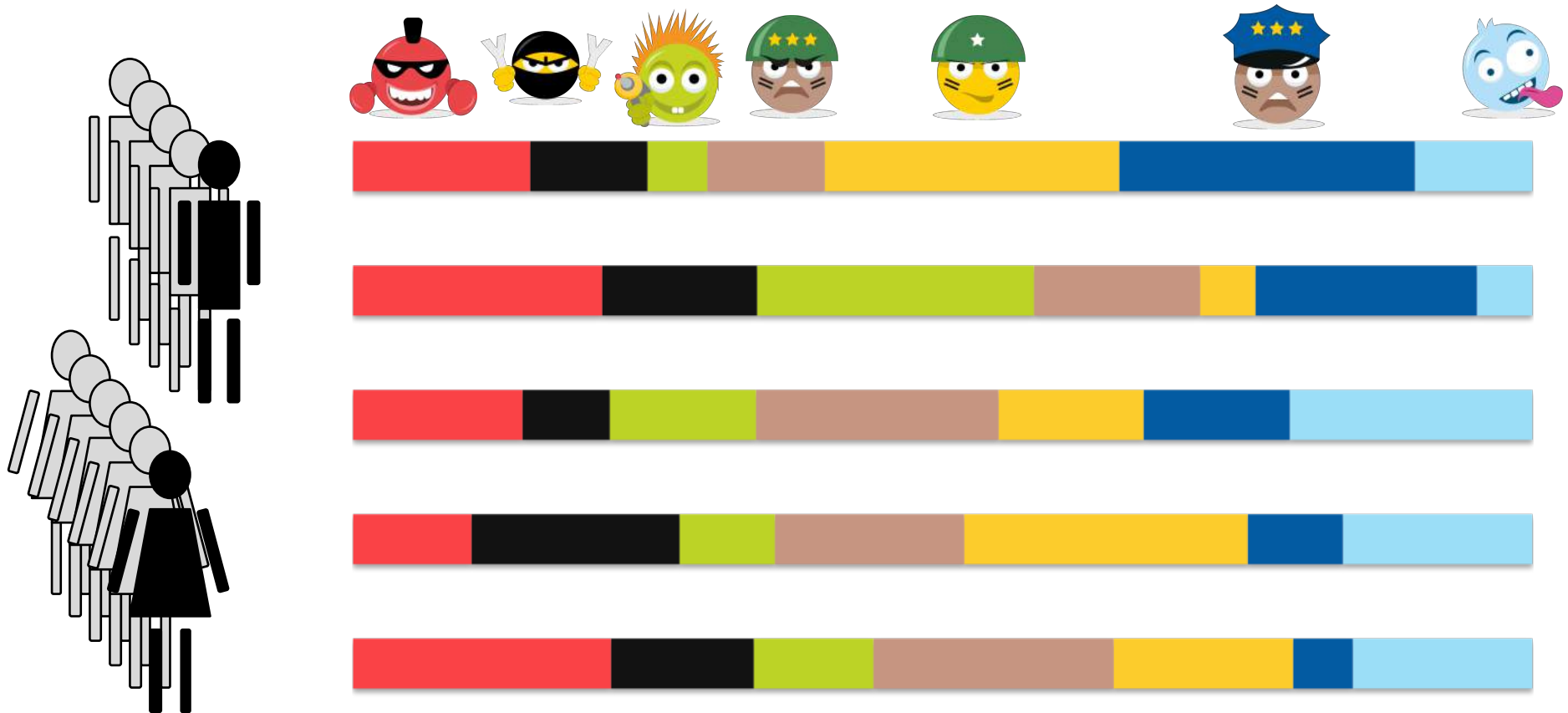
The immune system is composed of many cell types



The immune system is composed of many cell types that mount a coordinated attack on pathogens



Everyone 'fills the ranks' differently



What shapes the immune system?

- Genetics account for less than half of the variability of an immune profile
 - MZ vs. DZ twin study: estimate 23% genetic.
Brodin et al Cell **160**, 37-47 (2015)
 - Sardinian cohort QTL study: 41% genetic
Orru et al Cell **155**, 242-256 (2013)
 - ImmVar project, tested QTLs: 22% genetic.
de Jager Semin Immunol, (2015)
- Viral infections; CMV, EBV
- Ageing

What non-genetic factors shape the immune system?

670 healthy individuals

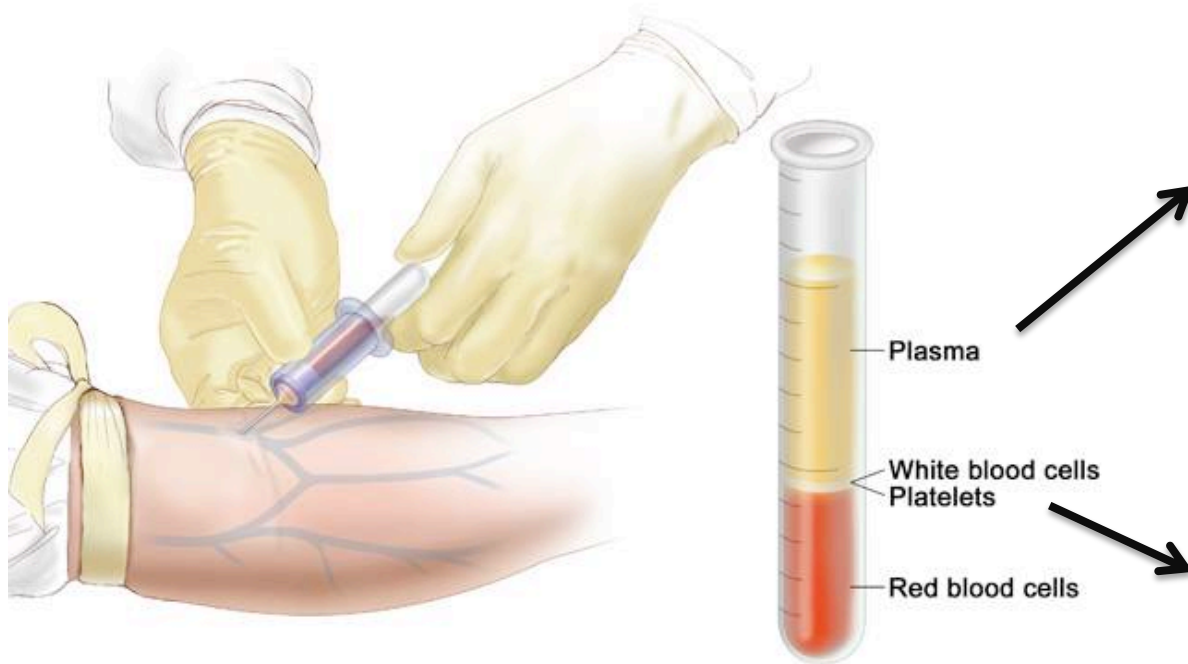
2-86 years of age

Longitudinal sampling of sub-cohorts

Correlations with non-genetic factors

- Age
- Body mass index (BMI)
- Co-parenting
- Gastroenteritis
- Vaccination
- Depression and anxiety

Our study



54 immunological parameters

MSD Serum analysis

Cytokines
Chemokines

Flow cytometry

CD4+ T cells
CD8+ T cells
NKT cells
B cells
Antigen presenting cells



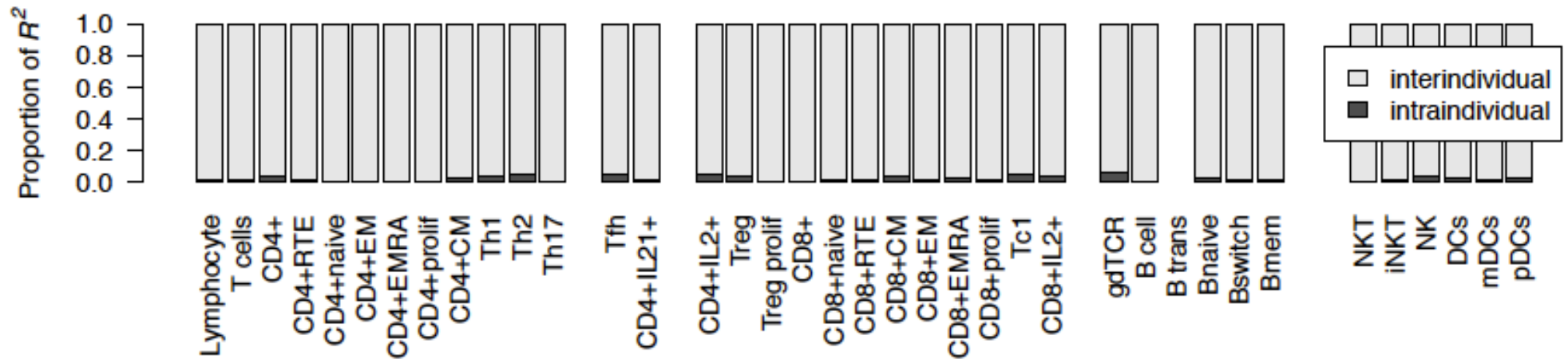
James Dooley
K.U. Leuven, Belgium

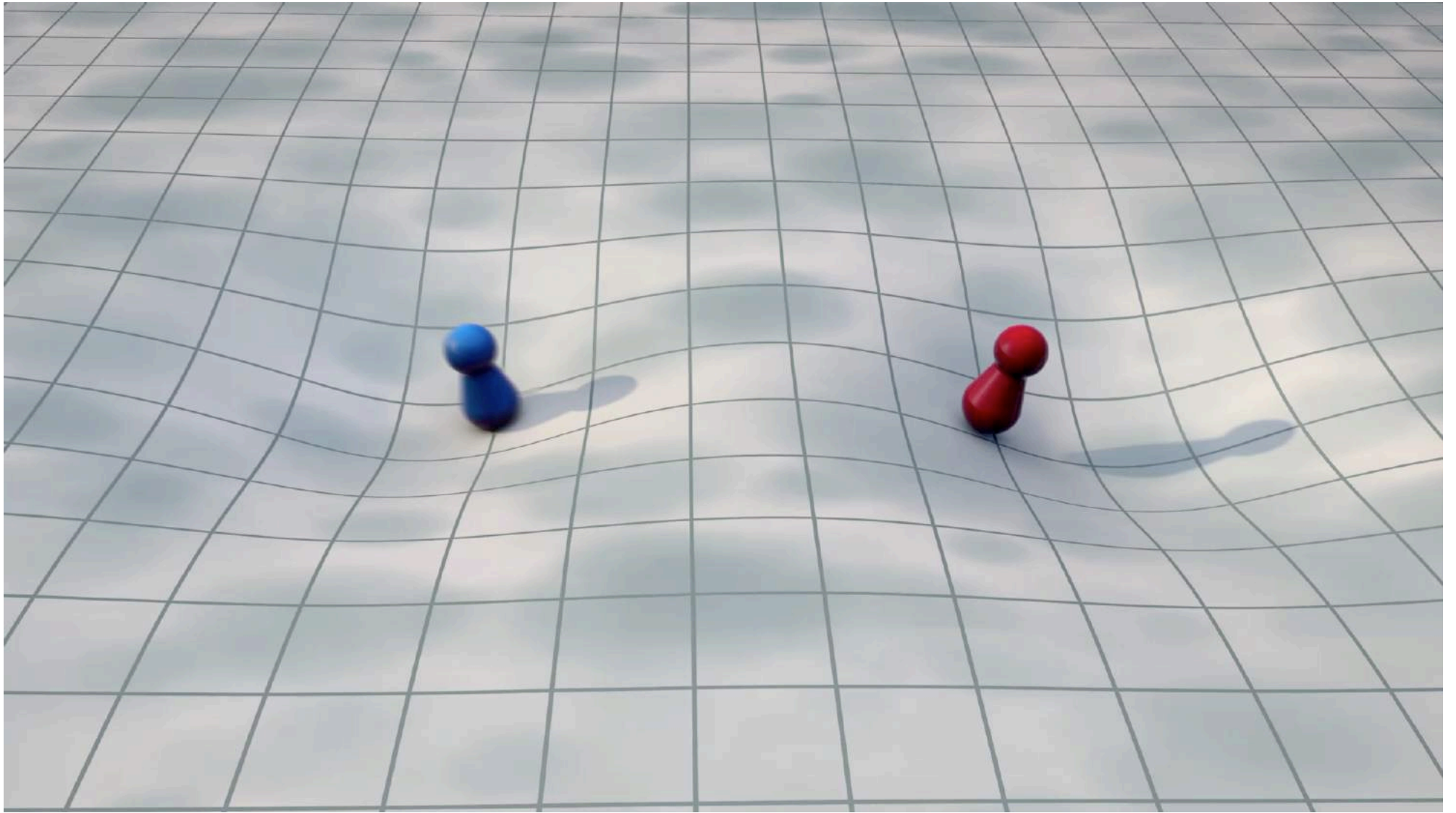


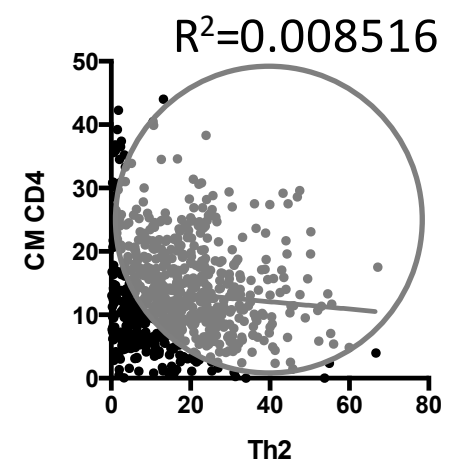
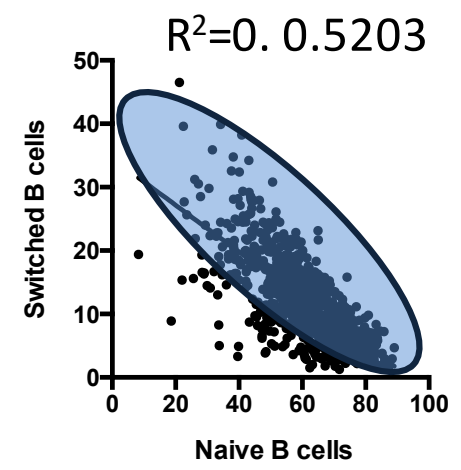
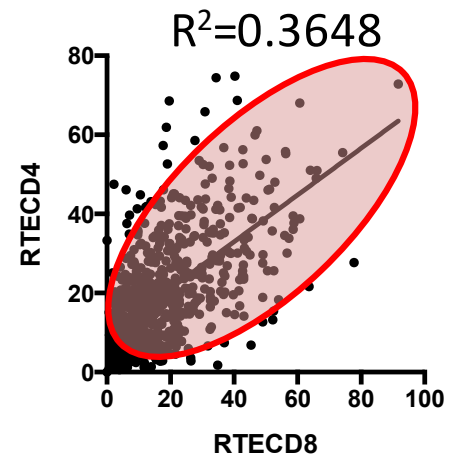
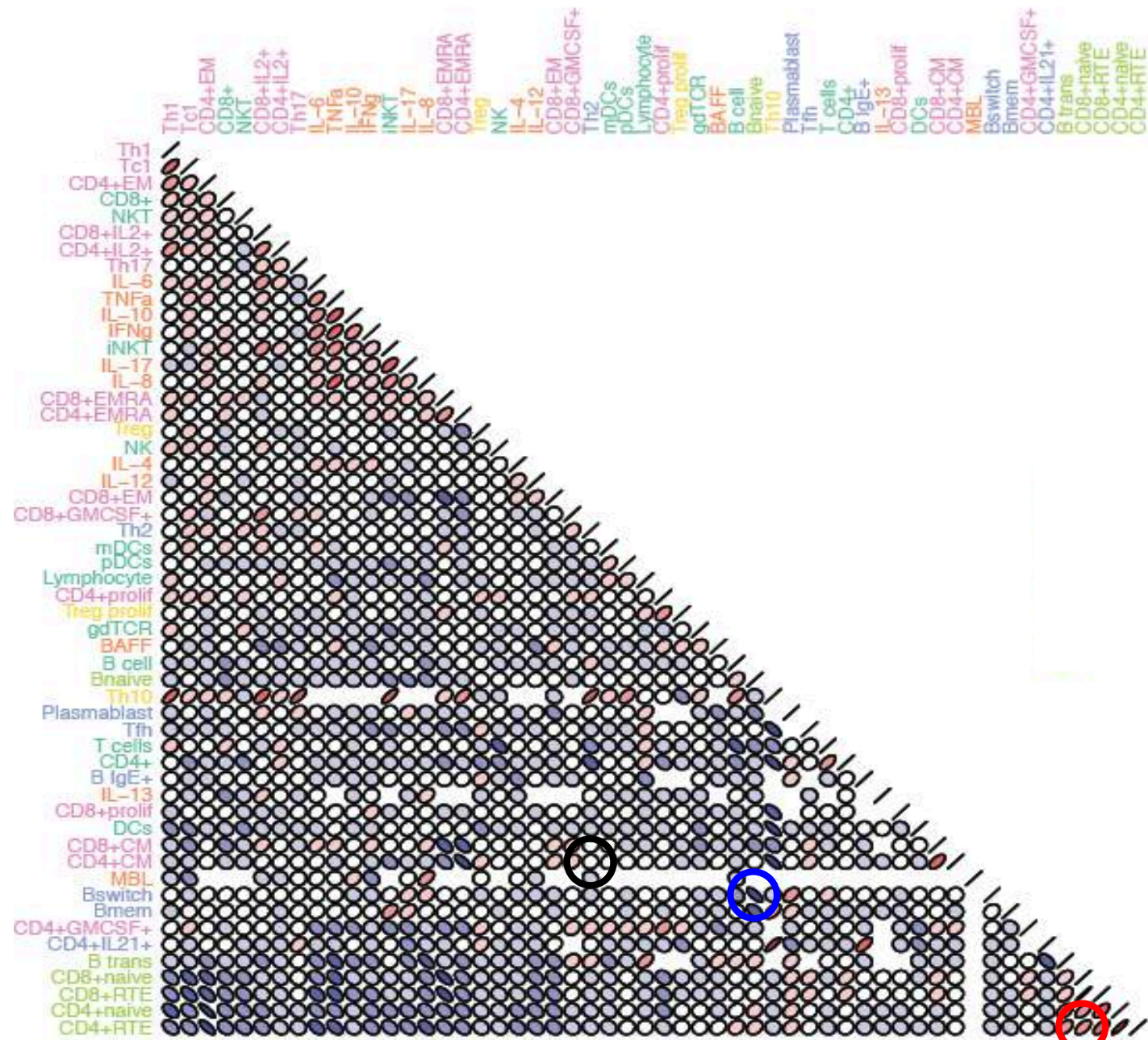
Edward Carr
Babraham Institute, UK

An individual's immune profile is stable over short time spans

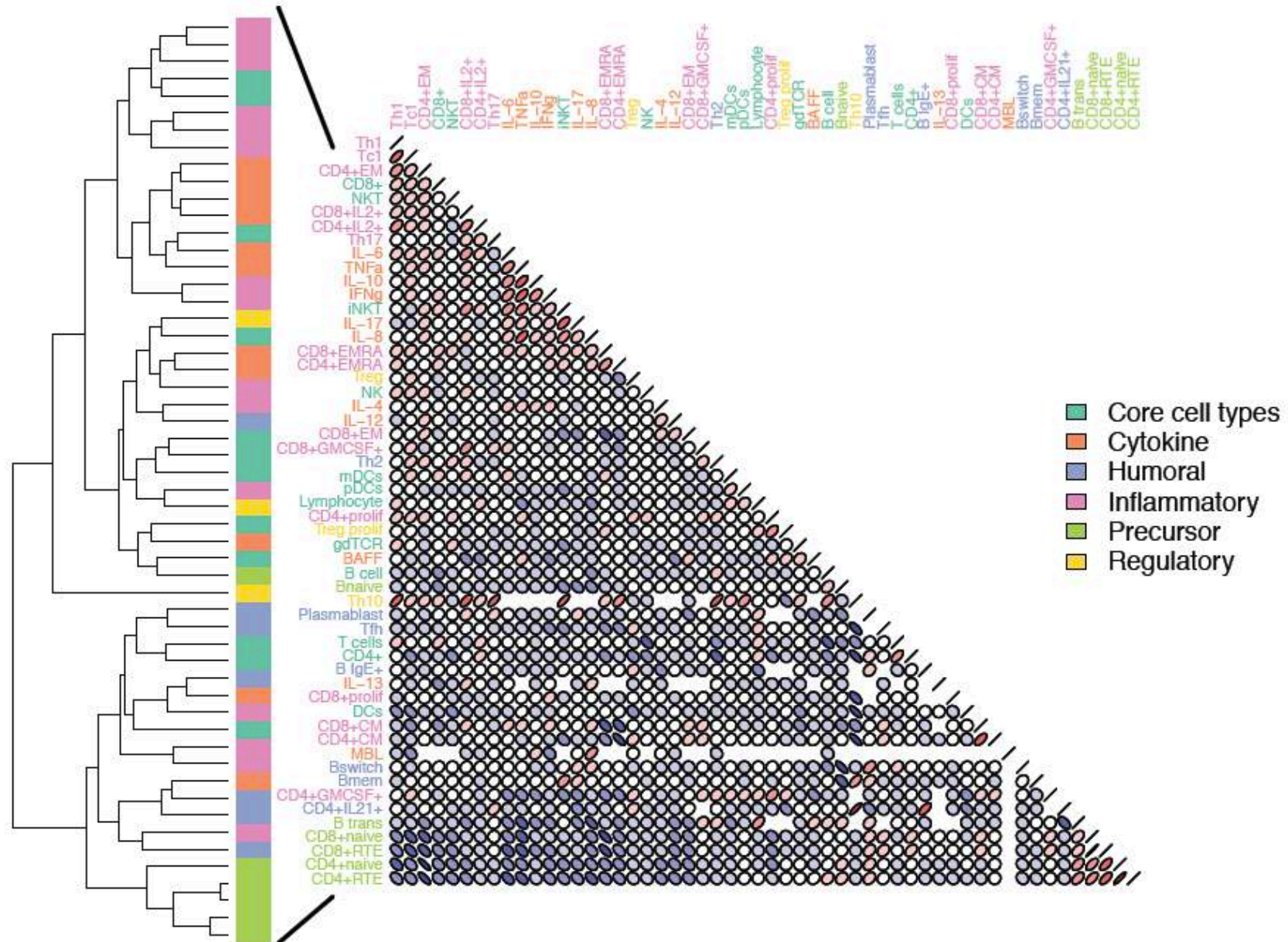
1.4% of variation is attributable to the intra-individual variation



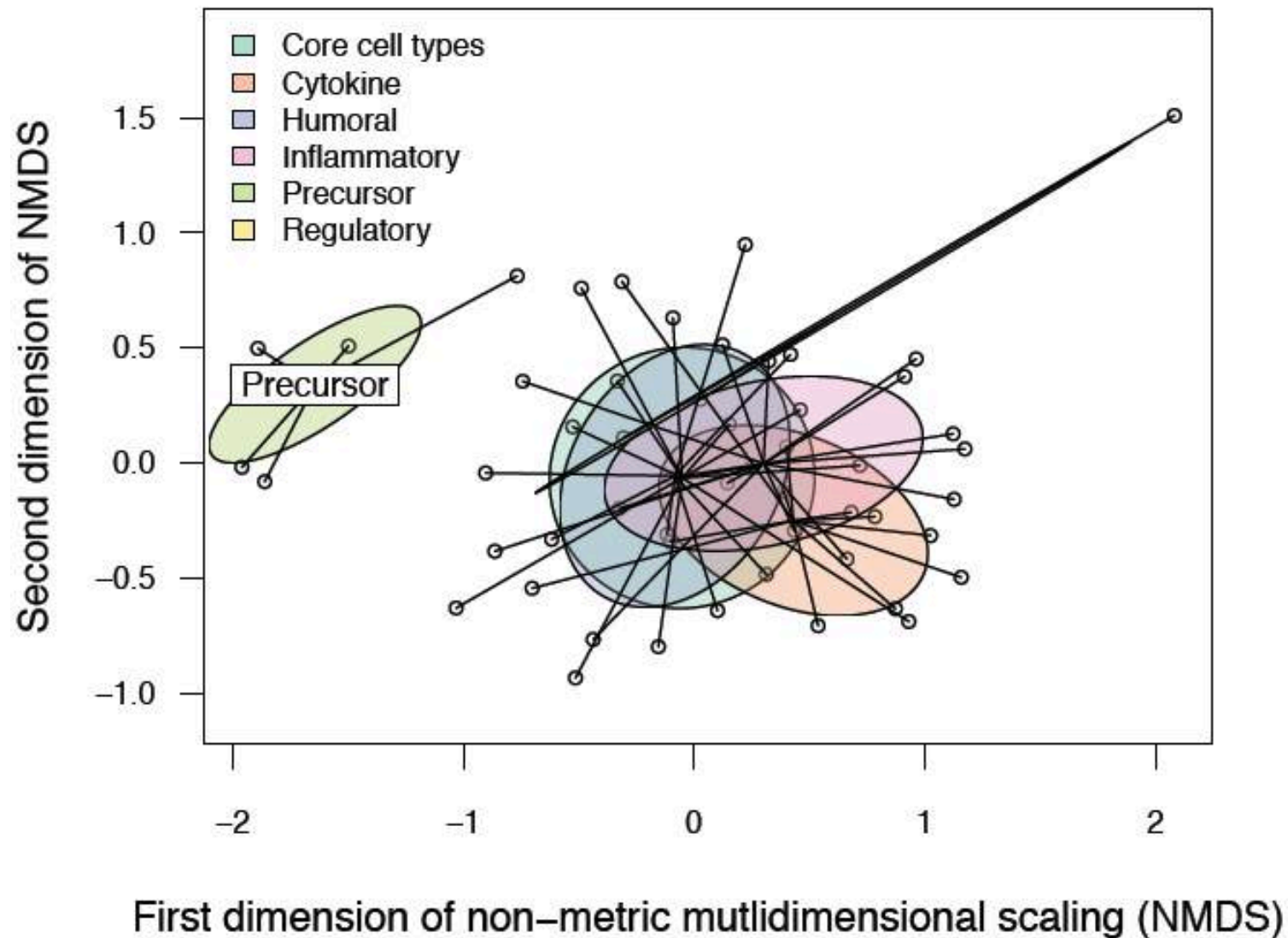


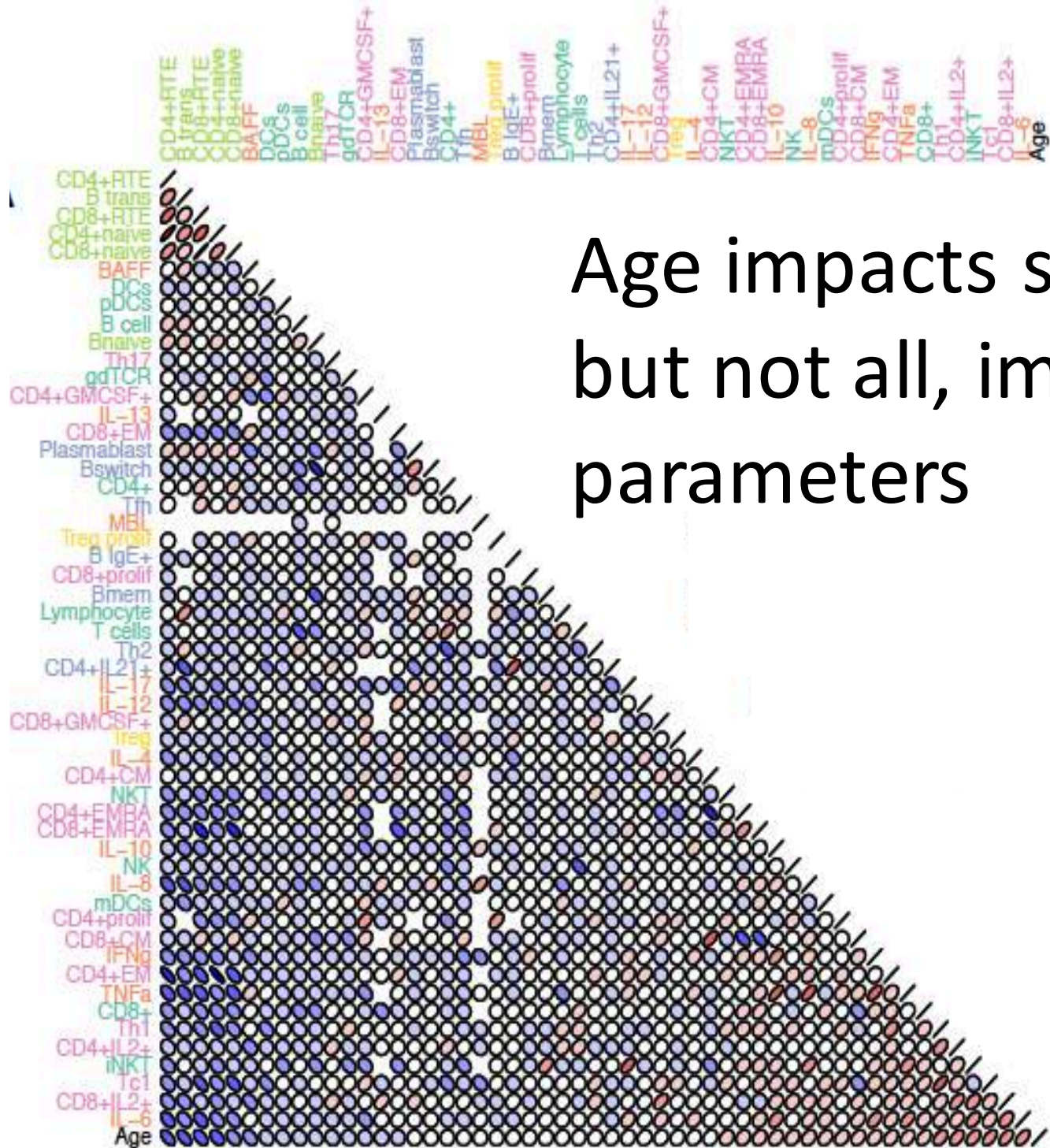


Precursor populations cluster together



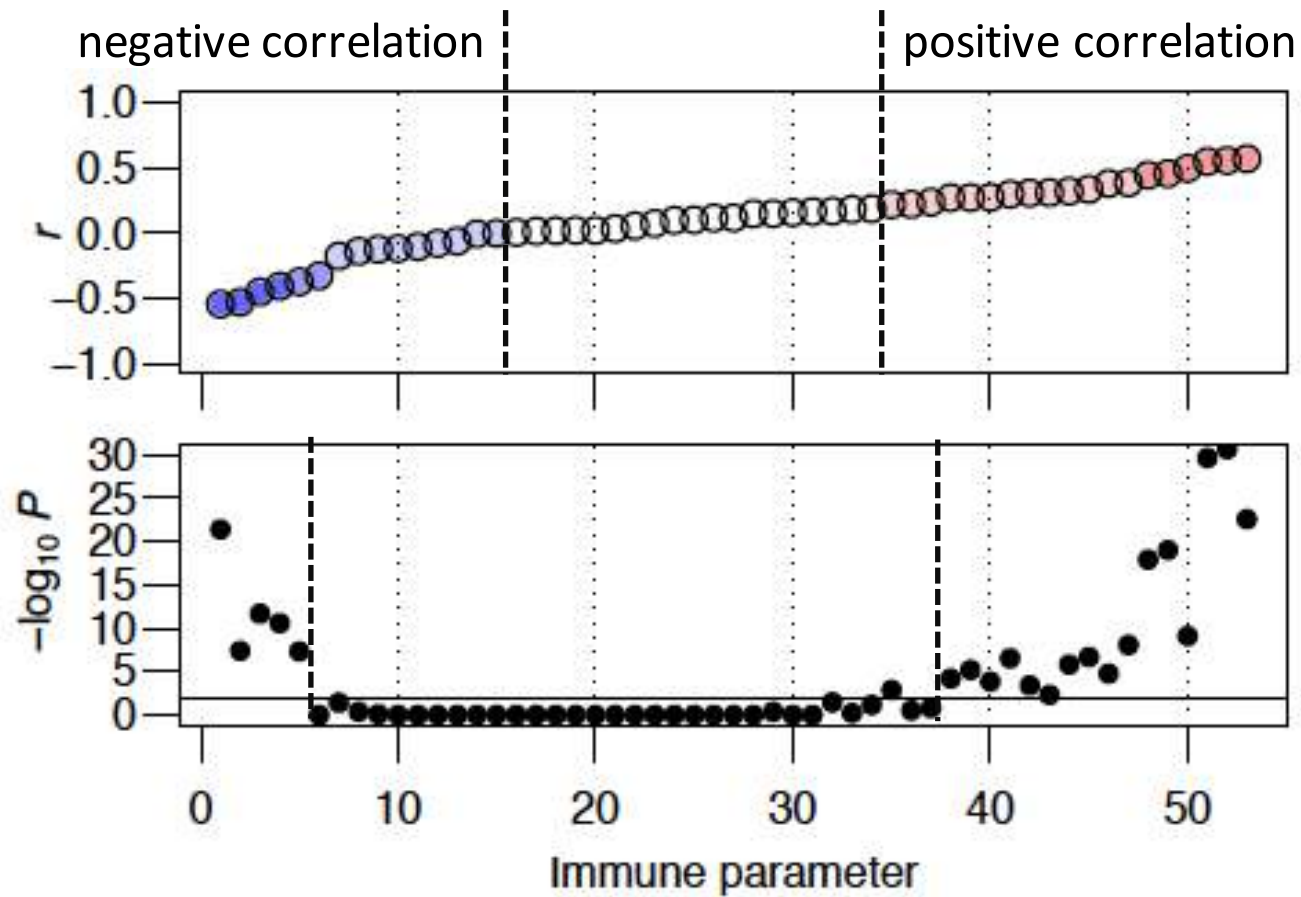
Precursor populations cluster together



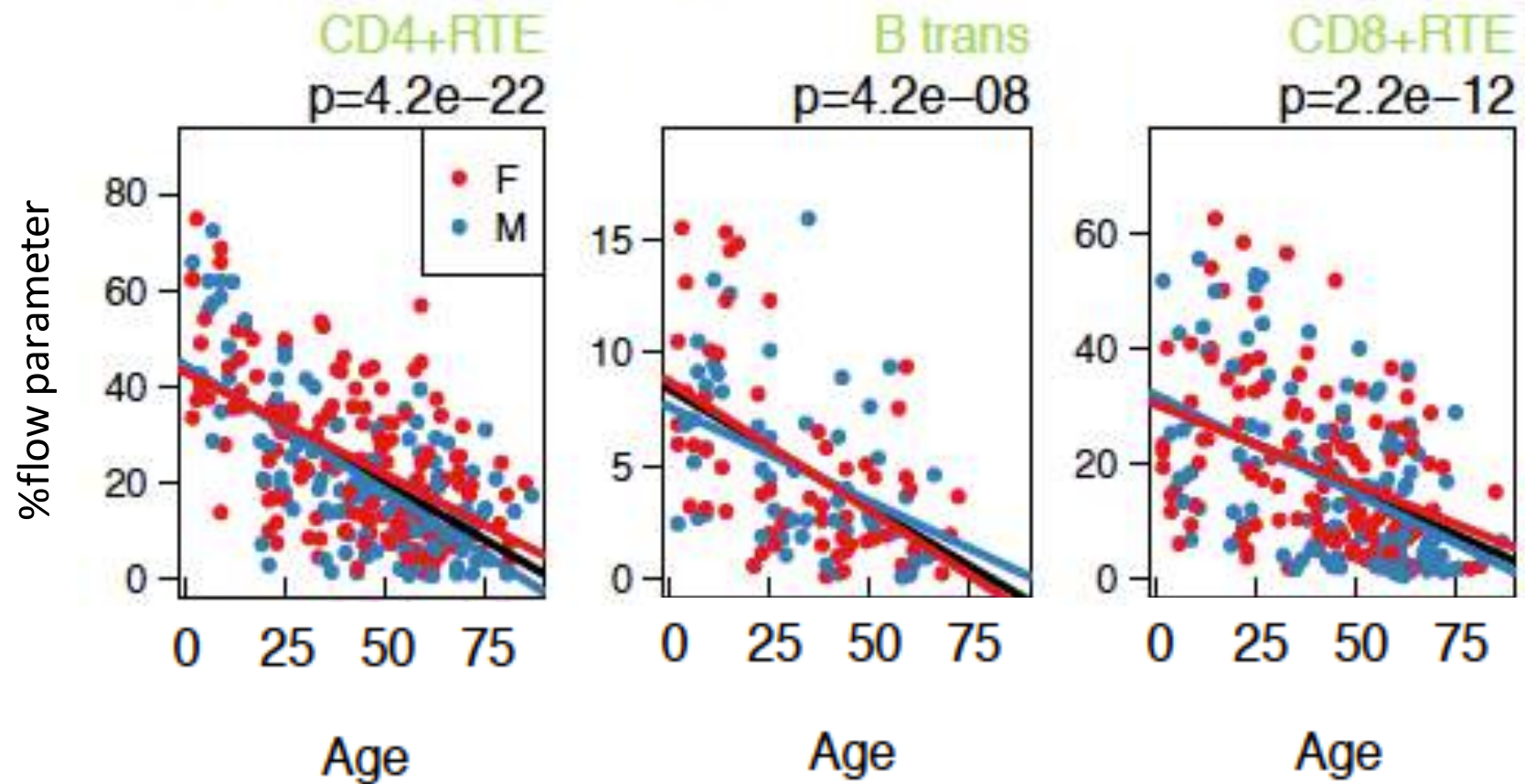


Age impacts some, but not all, immune parameters

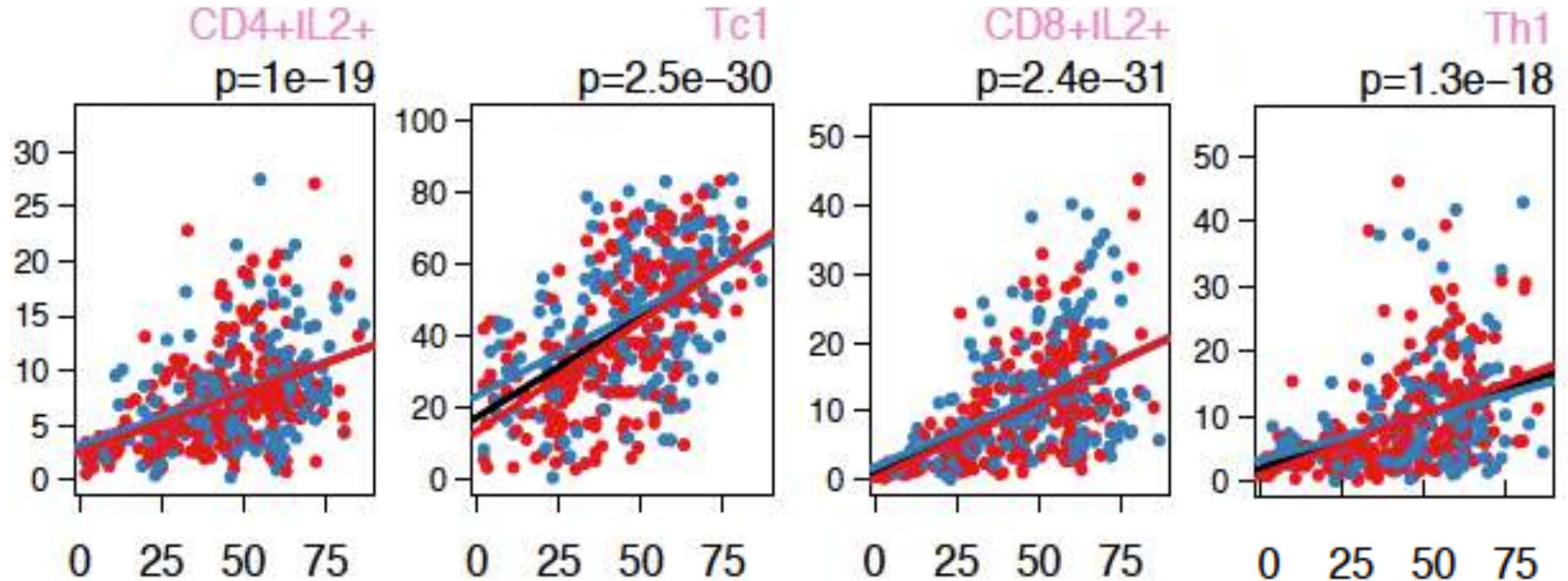
There are strong relationships between immune parameters and age



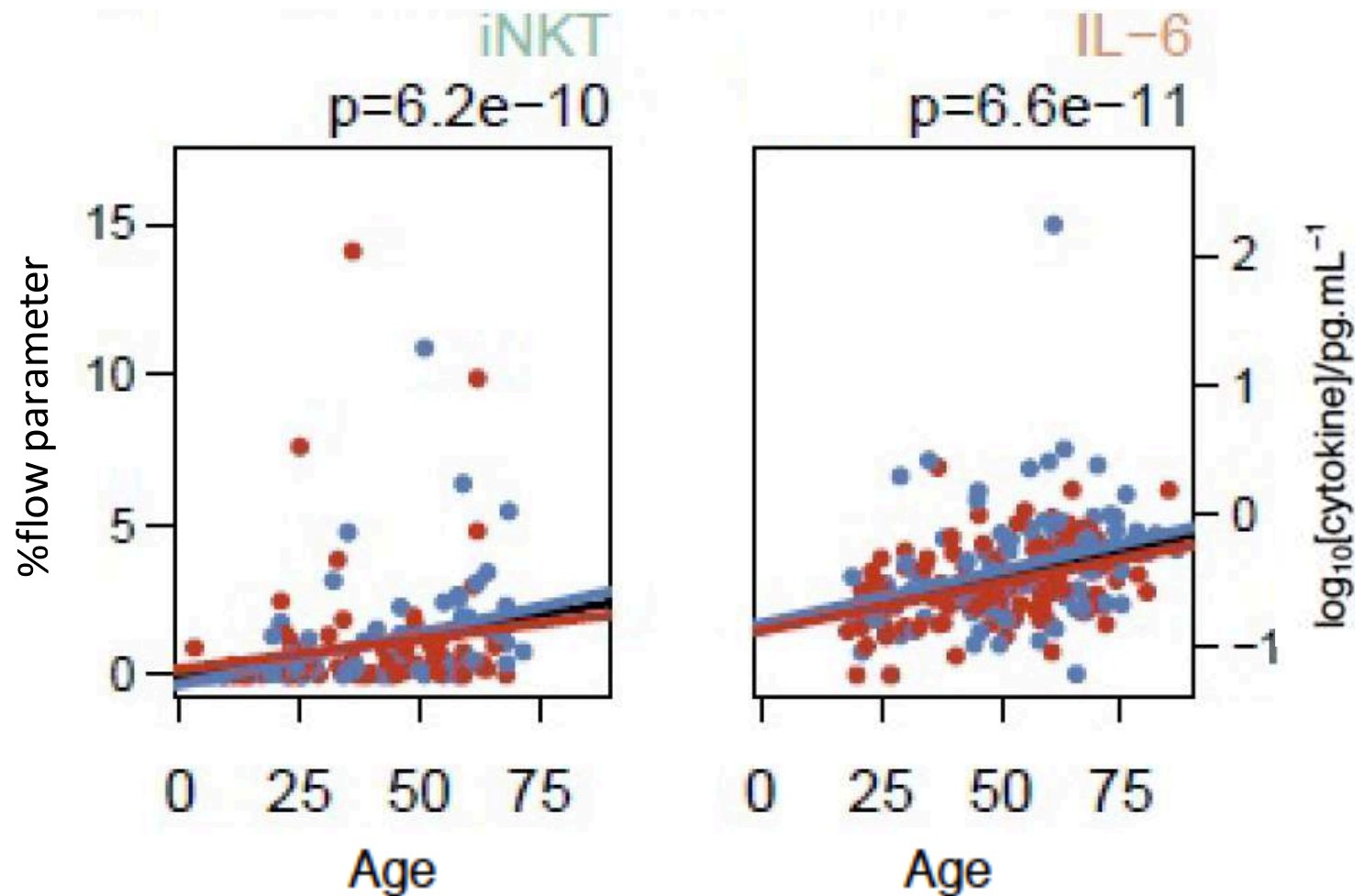
Precursor populations negatively correlate with age

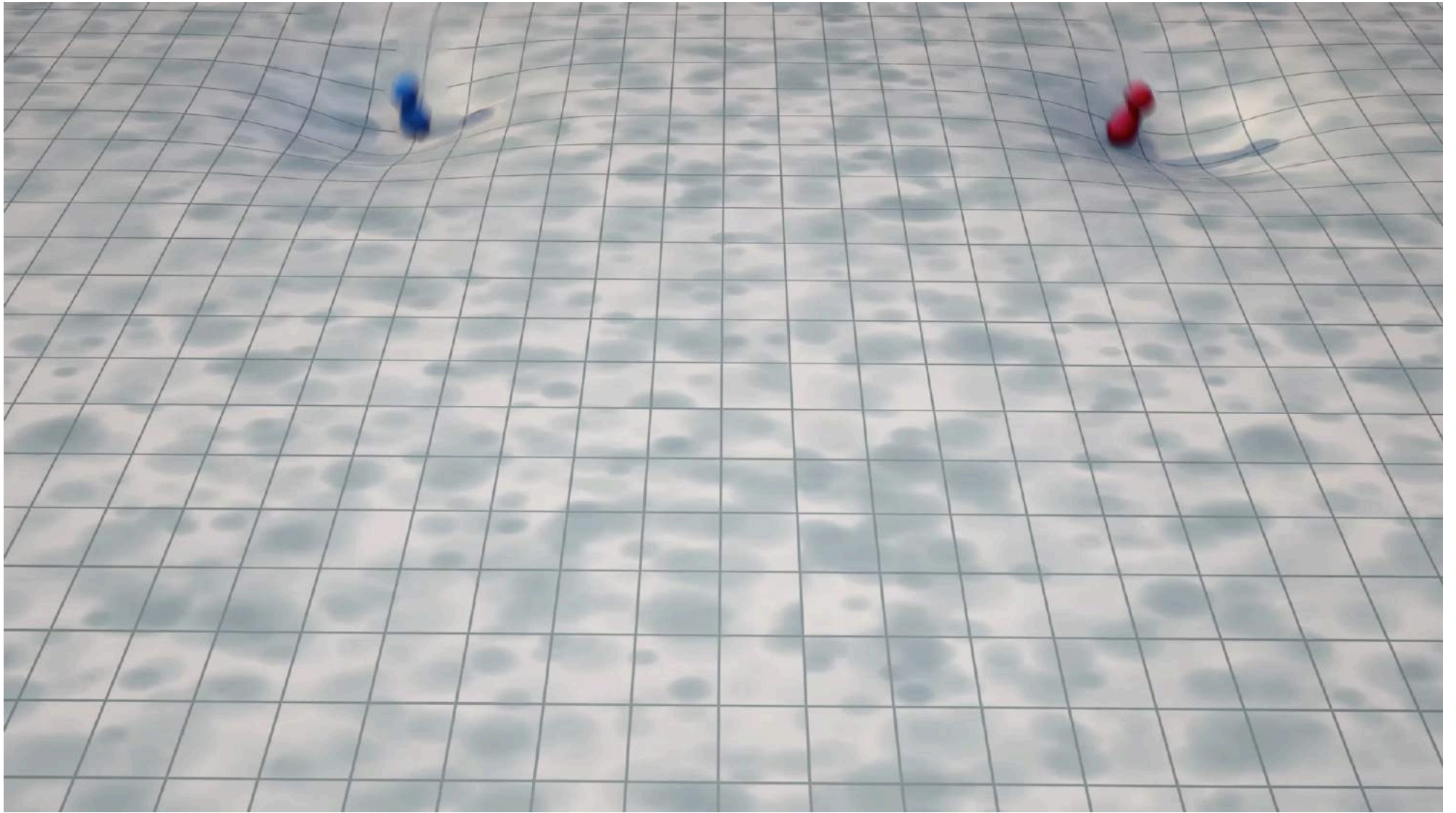


IFN γ ⁺ and IL-2⁺ populations positively correlate with age

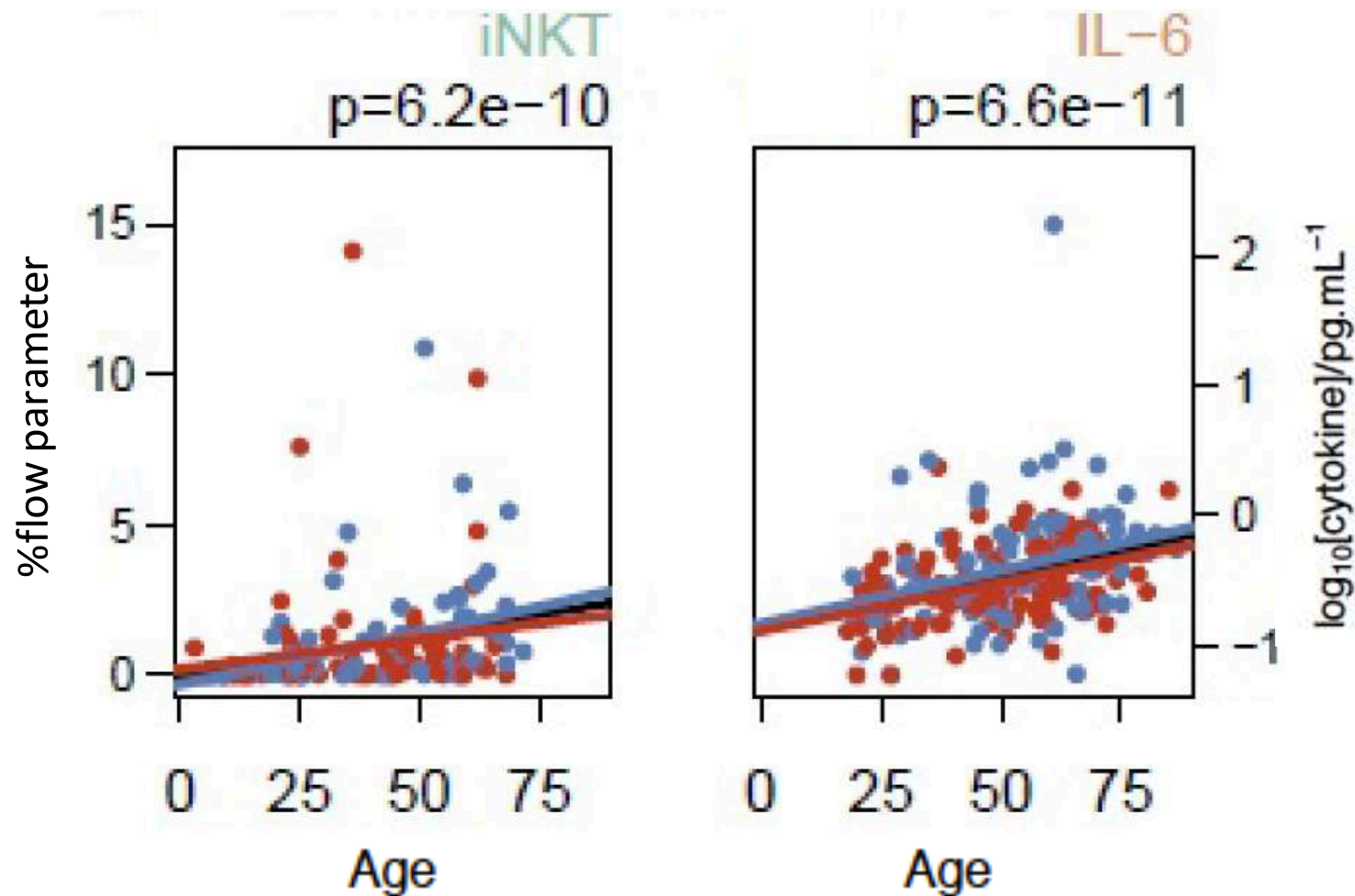


iNKT cells and serum IL-6 positively correlate with age

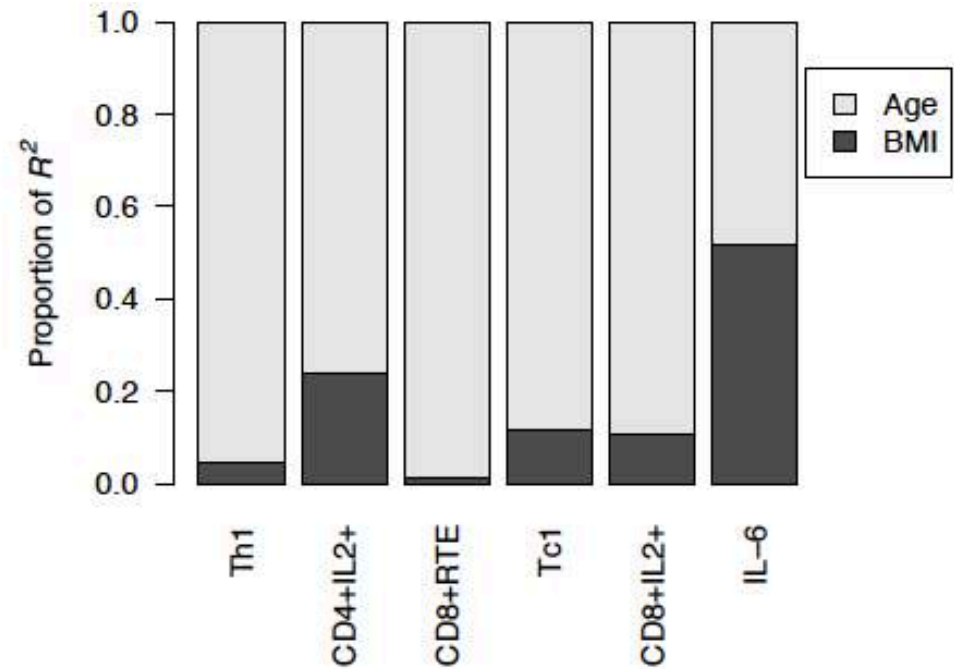
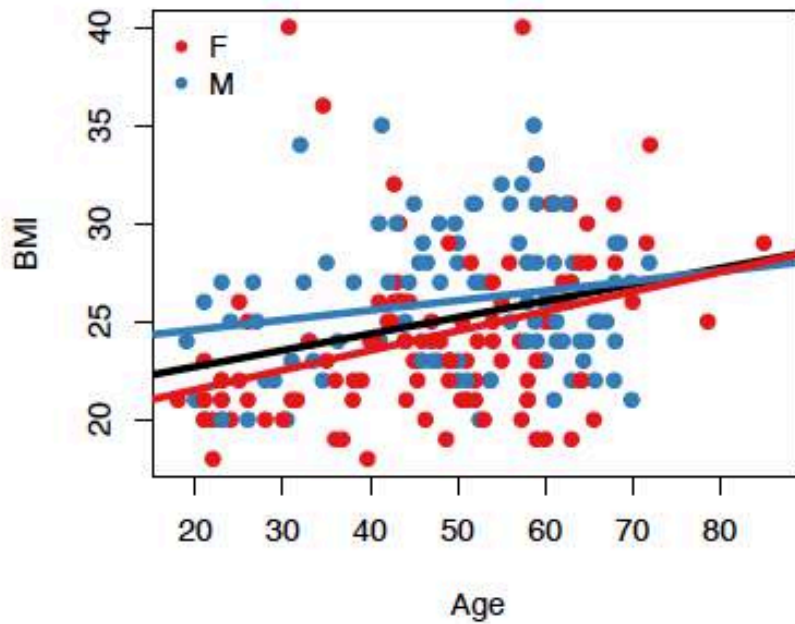




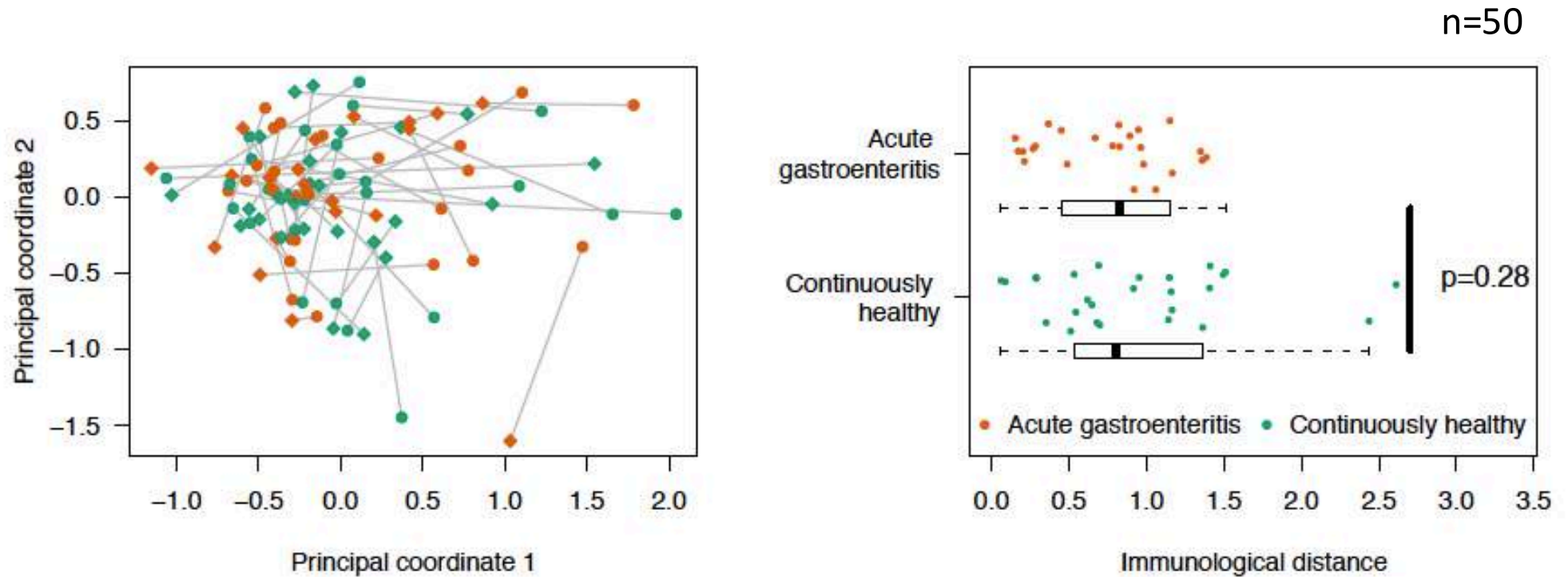
iNKT cells and serum IL-6 positively correlate with age



Does BMI play a role in age-dependent immune profiles?

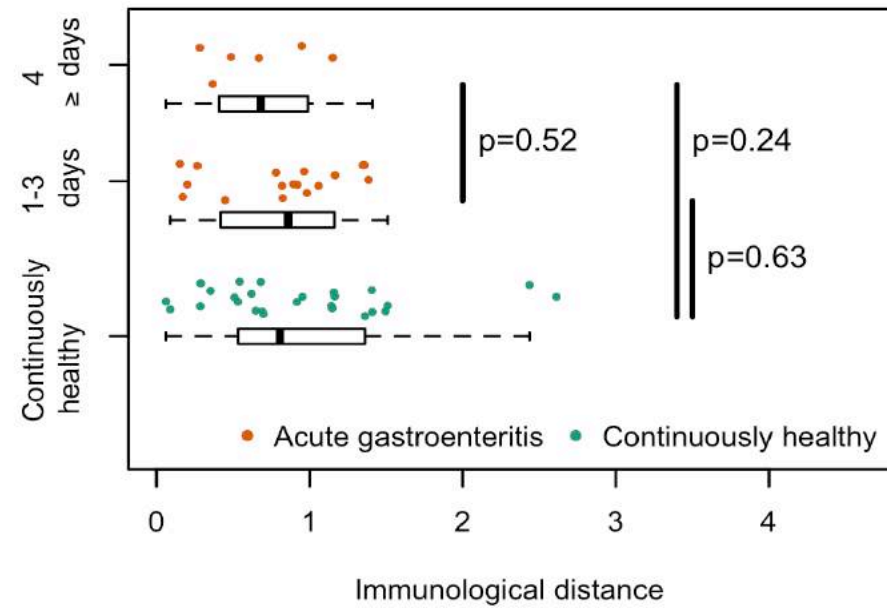
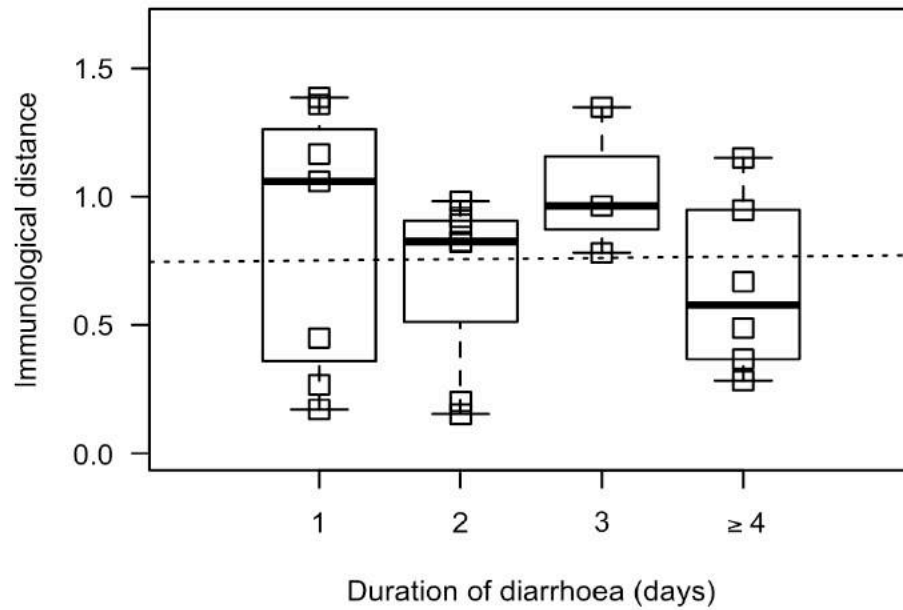


Acute gastroenteritis does not perturb the immune landscape

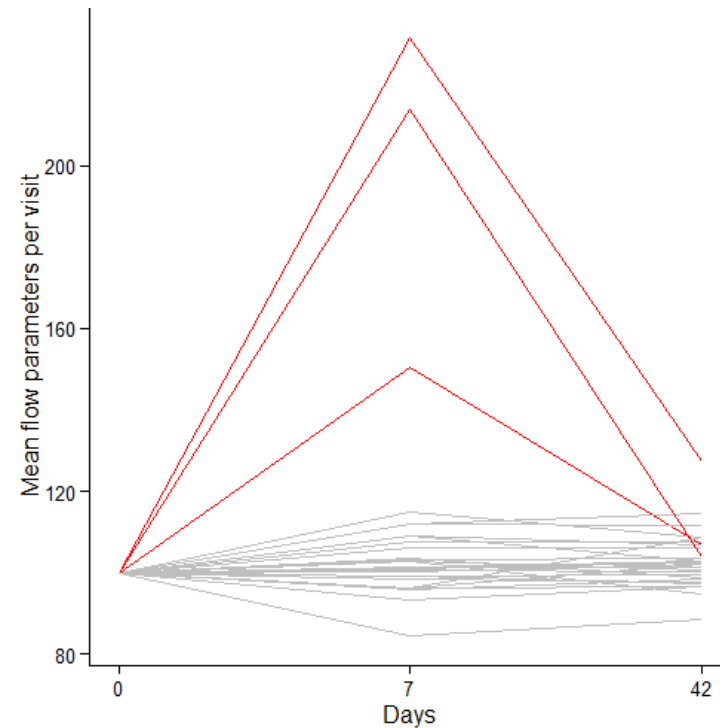
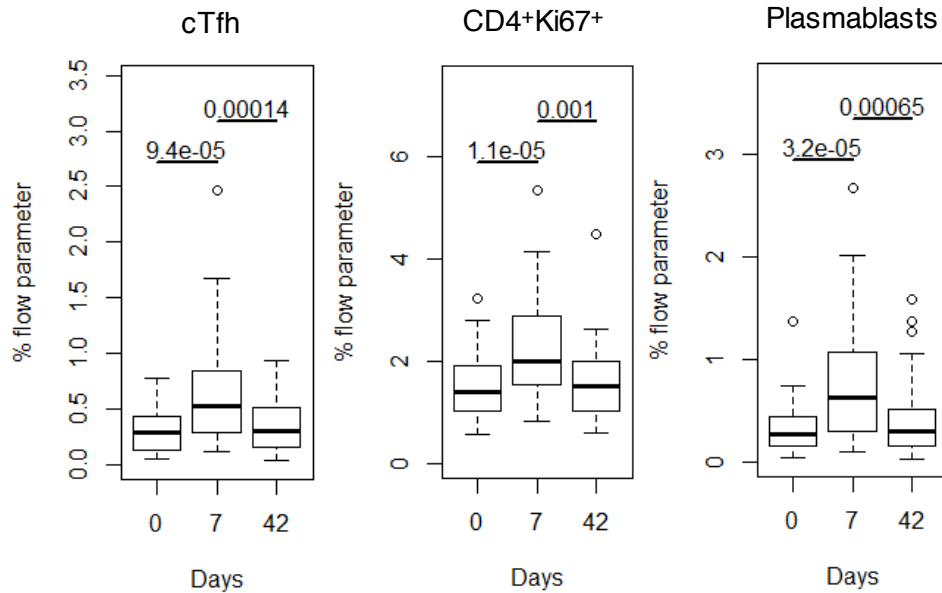
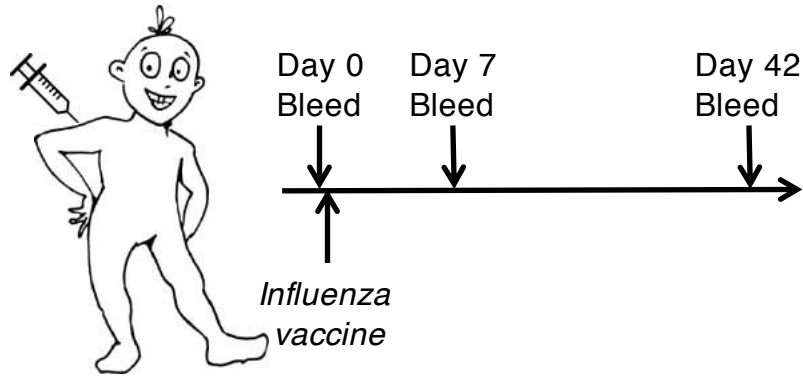


- Pre-travel (healthy)
- ◆ Post-travel (healthy, n=26)
- Pre-travel (acute gastroenteritis)
- ◆ Post-travel (acute gastroenteritis, n=24)

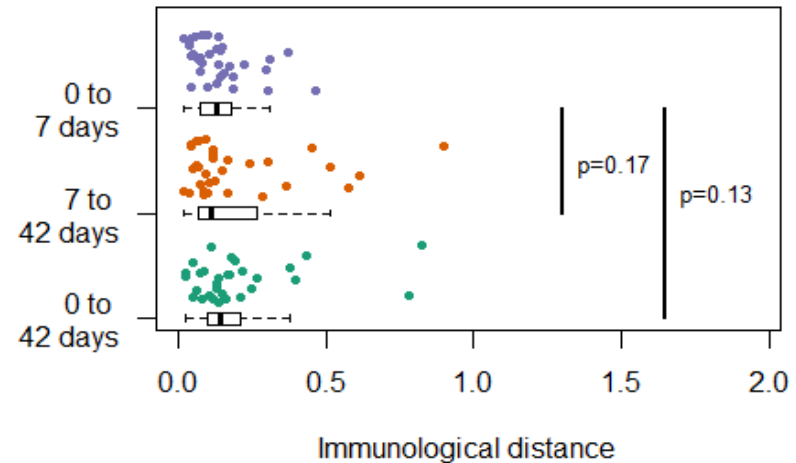
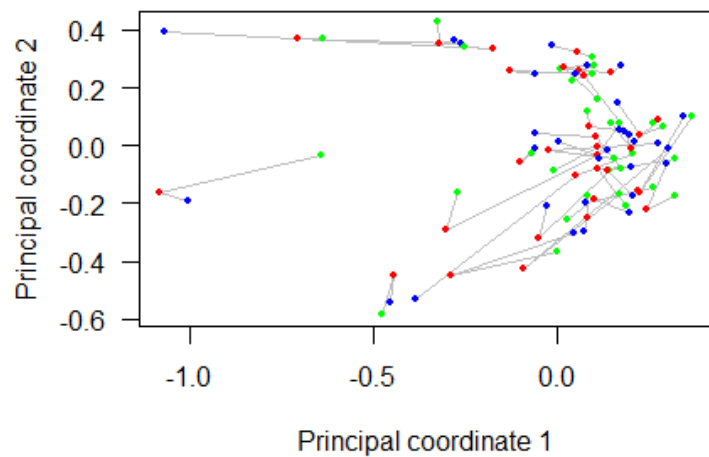
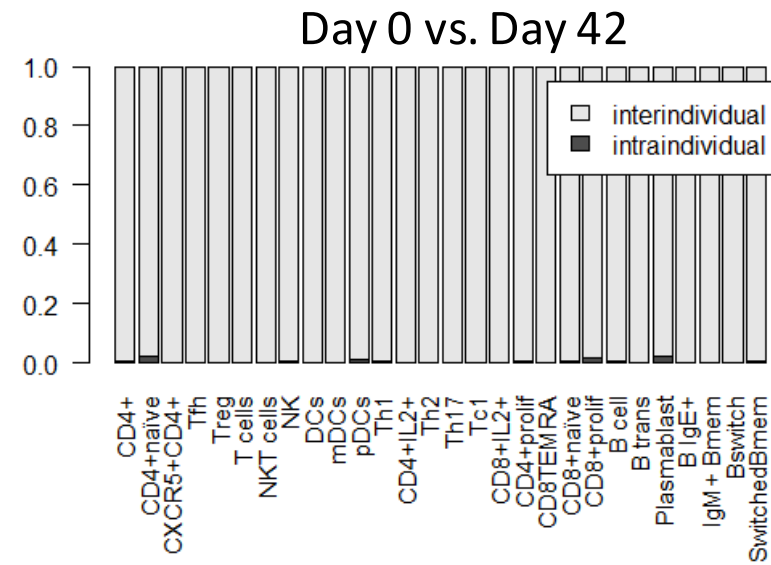
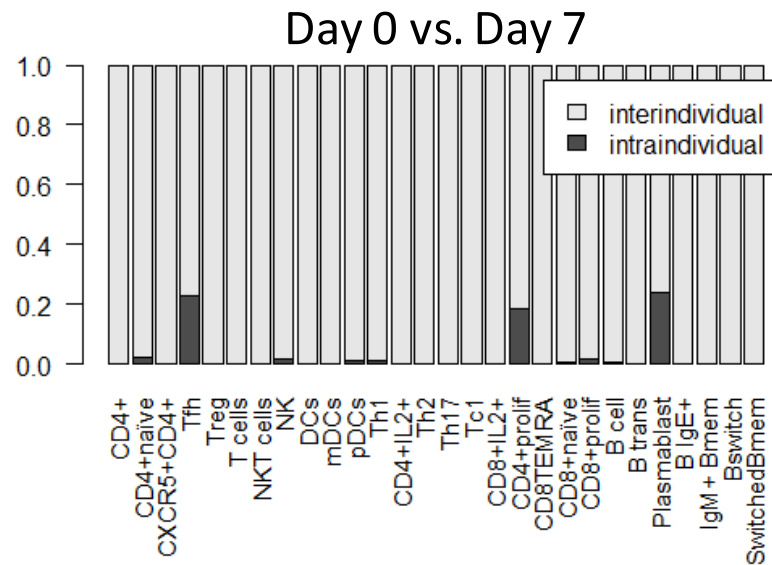
Length of gastroenteritis does not alter immunological distance

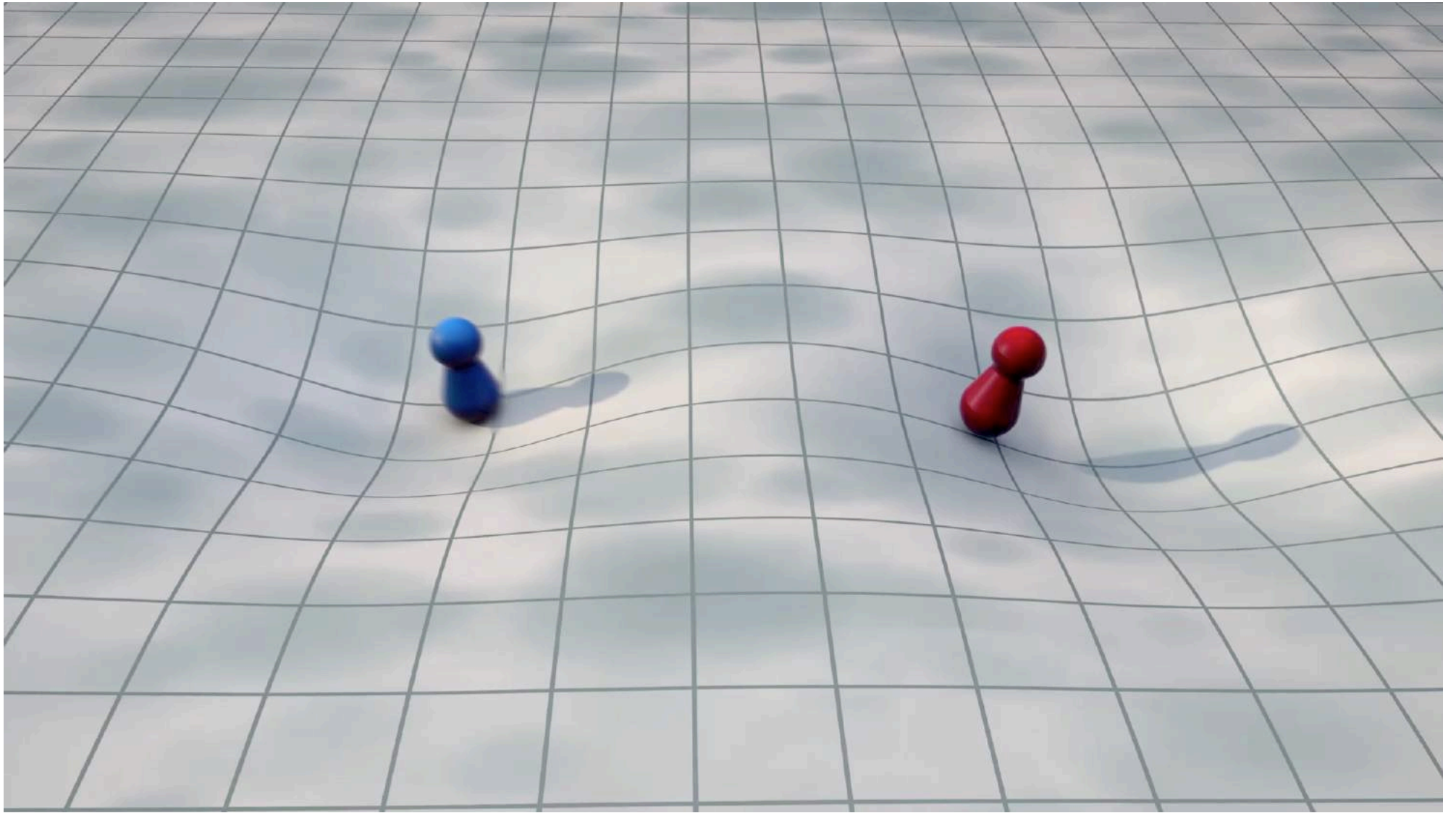


Vaccination temporarily perturbs the immune landscape

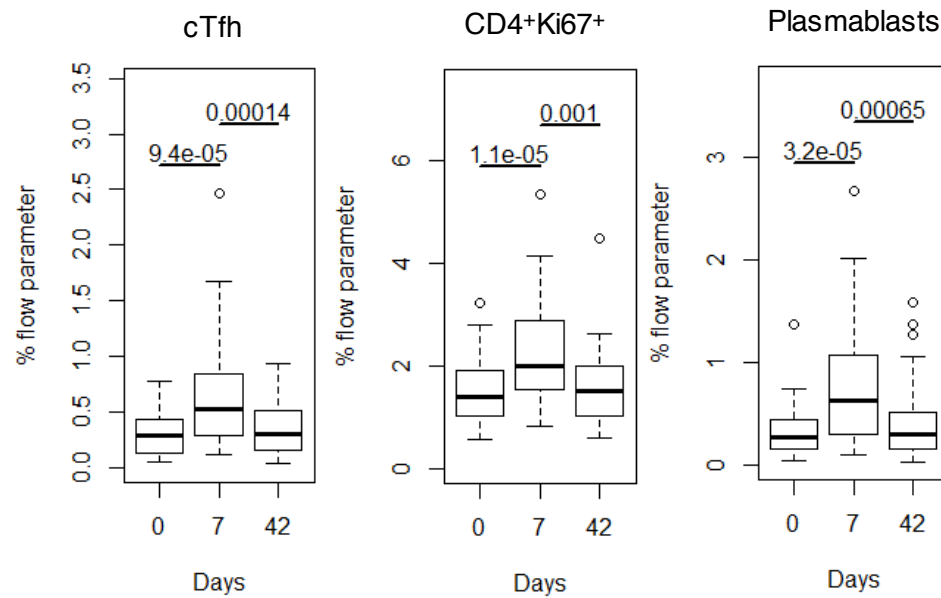


Vaccination temporarily perturbs the immune landscape

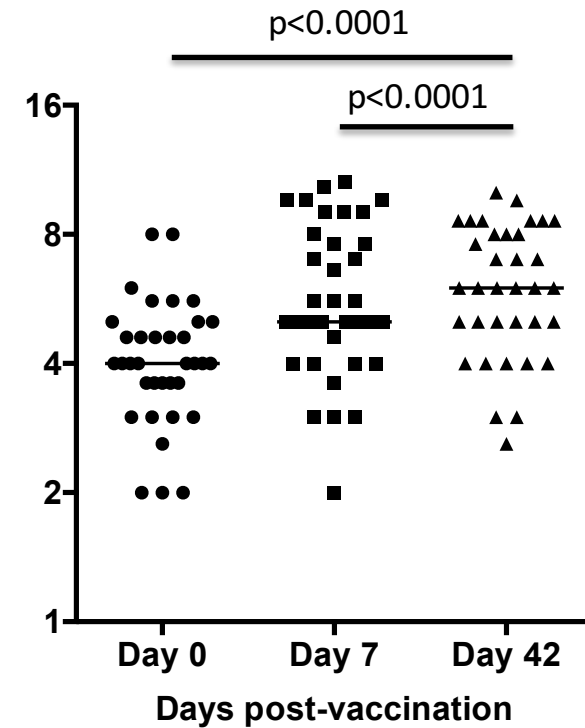




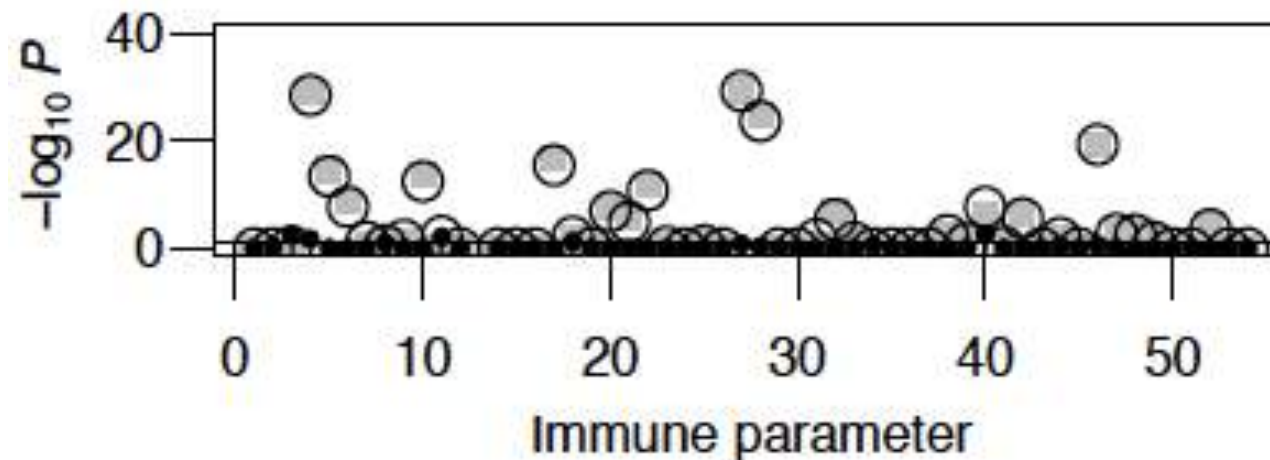
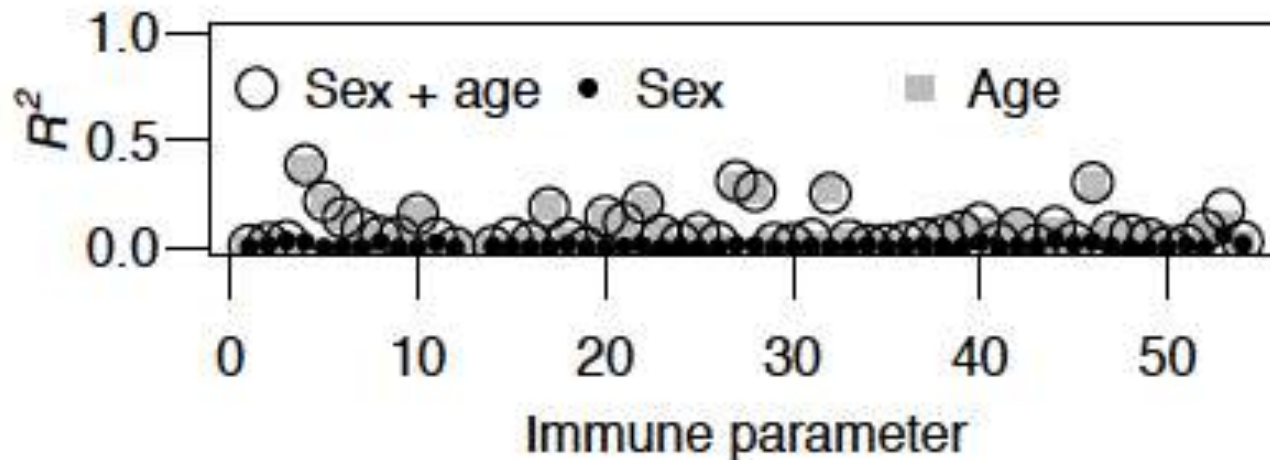
Antibodies provide protection after vaccination



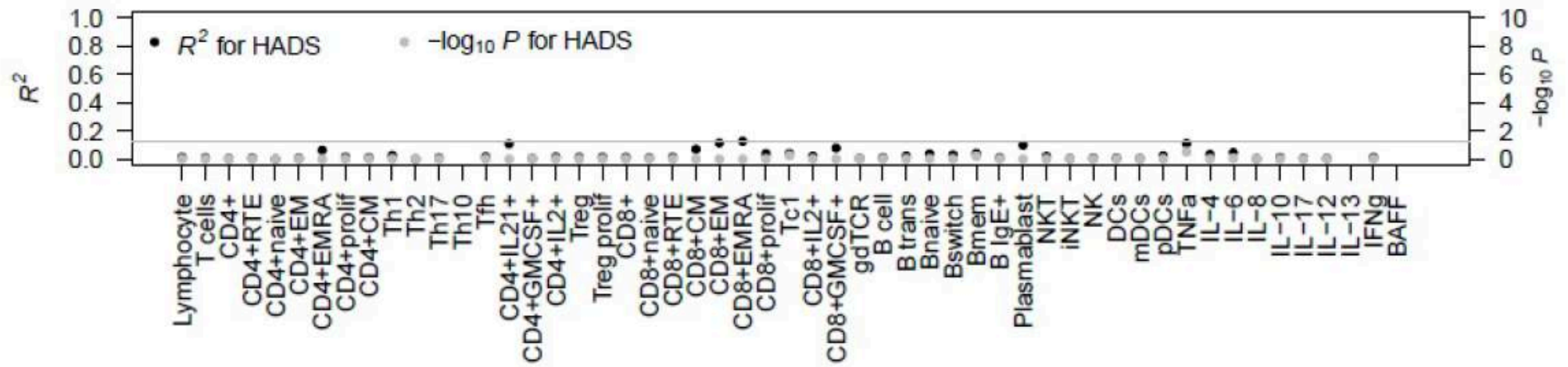
Neutralising antibody titre (HAI Log₂)



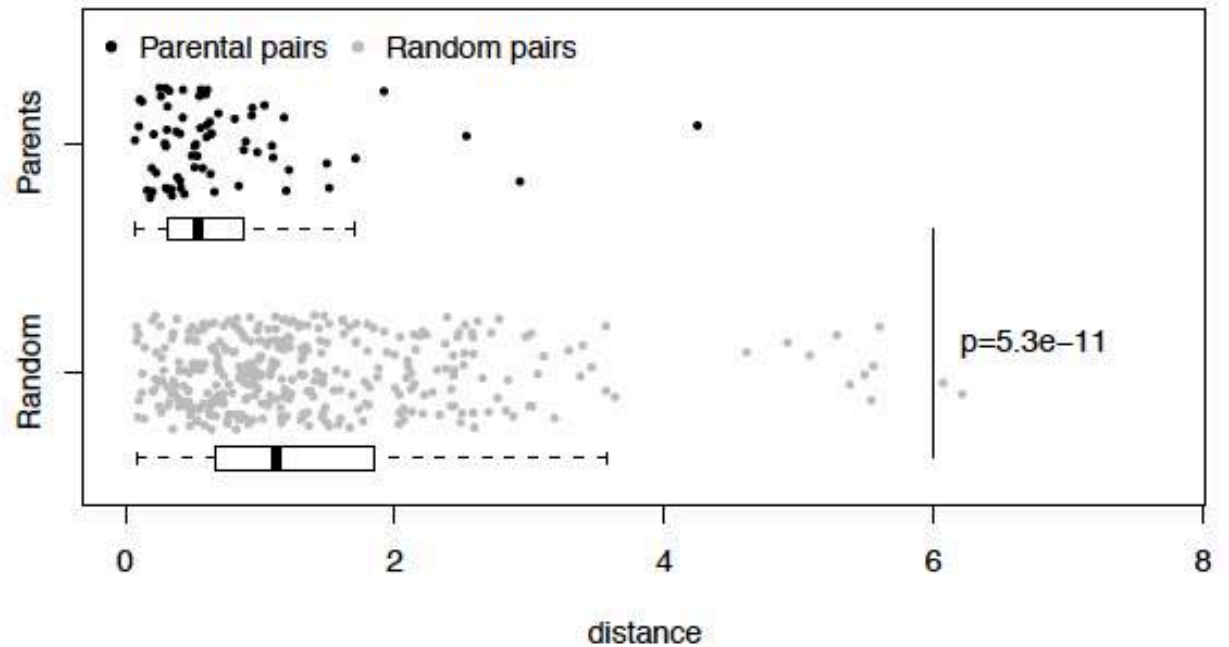
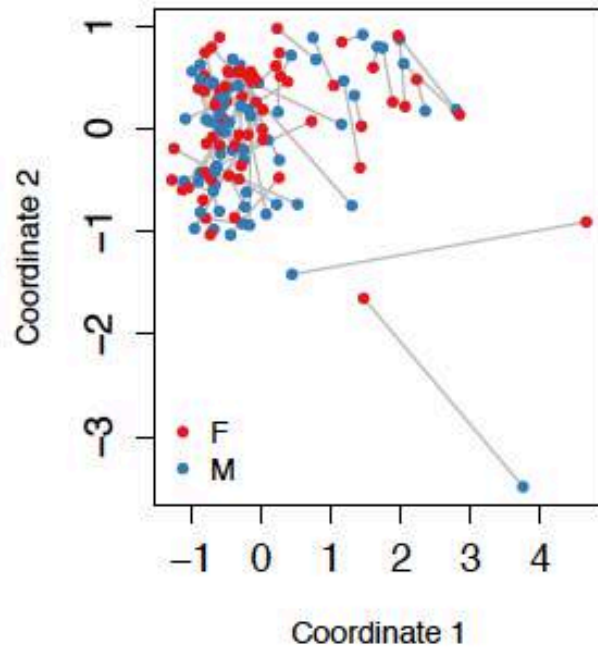
Gender does not significantly contribute to age-dependent immune changes



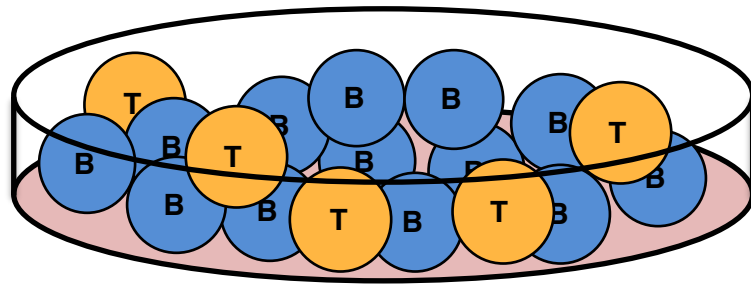
There is no relationship between Anxiety and depression scores (HADS) and immune parameters



Co-parents have a similar immune profiles



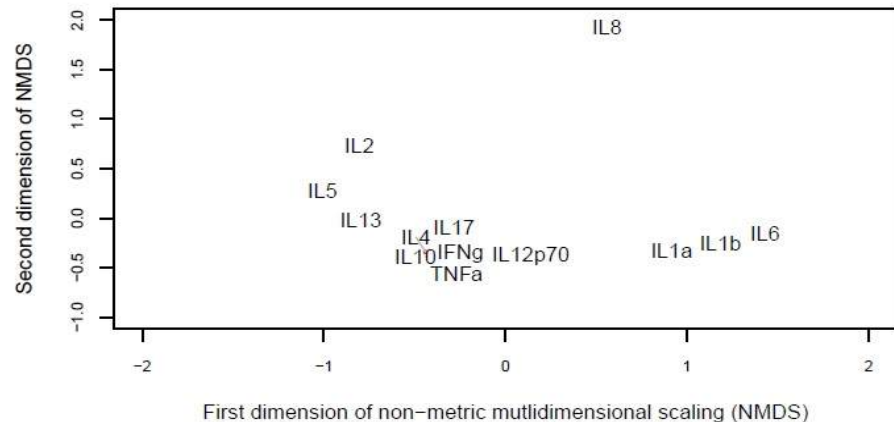
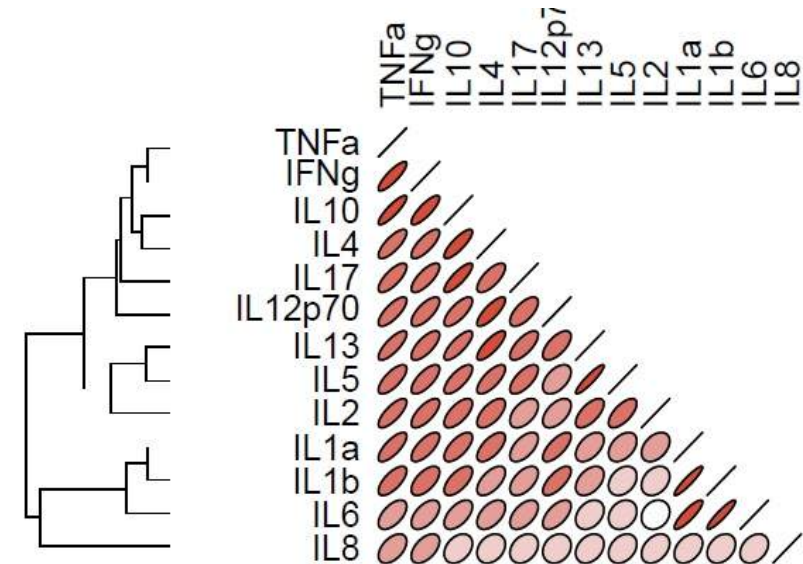
T cell cytokine production recapitulates immunophenotyping findings



24hrs CD3/CD28 stimulation

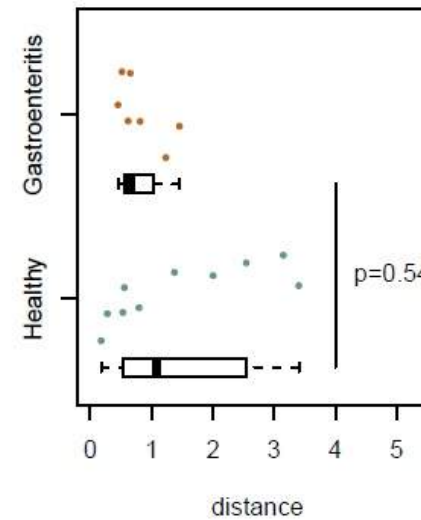
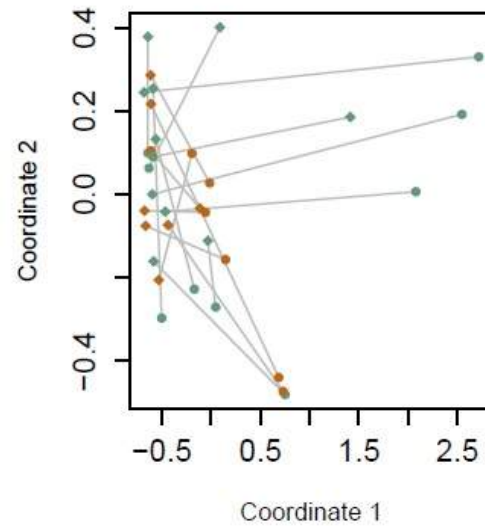


Assess serum cytokines

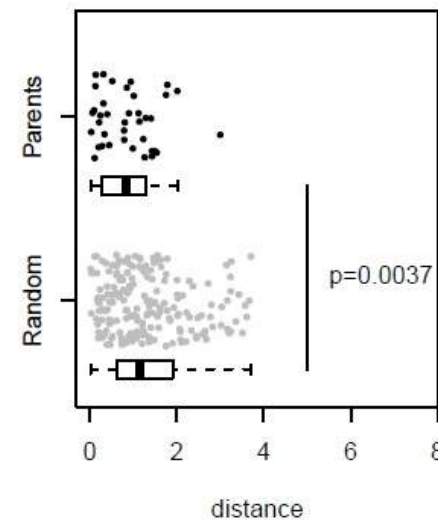
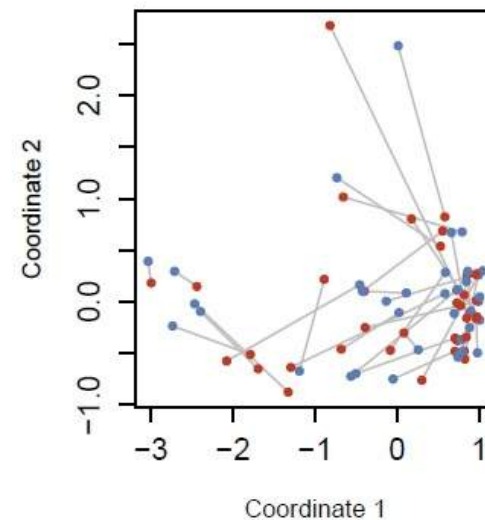


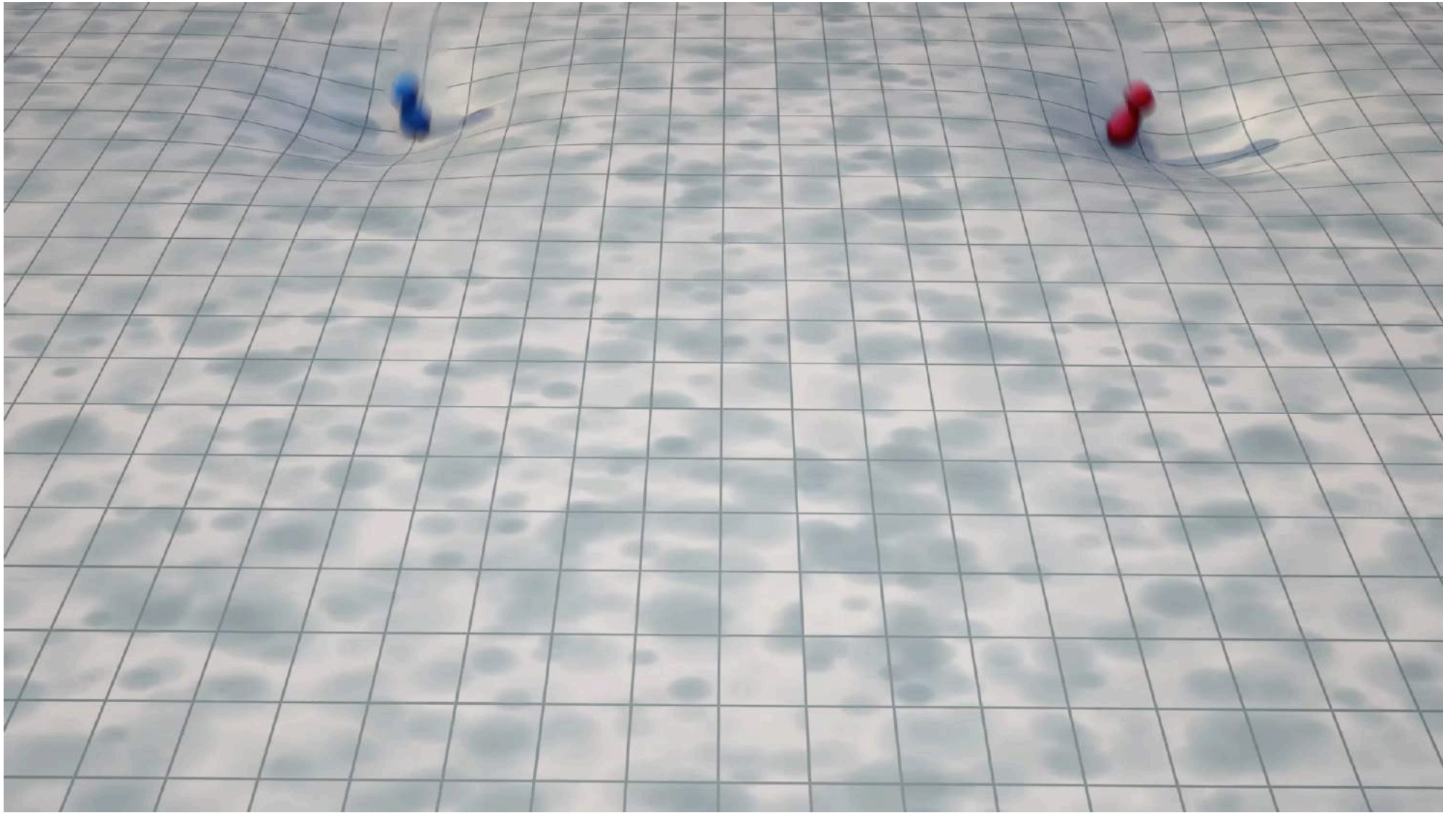
T cell cytokine production recapitulates immunophenotyping findings

Gastroenteritis



Parental pairs





The human immune system

- Age is one of the biggest drivers of change
 - not all cell types are influenced by age
 - A linear model best fits the changes in the immune profile with age
- Acute gastroenteritis does not perturb the immune landscape
- Vaccination transiently alters some immune parameters
- Co-parenting influences immune profiles

The **NIHR Cambridge BioResource** is a resource of ~16,000 volunteers, both **with** and **without health problems**, who are willing to be approached to **participate in research studies** investigating the links between **genes, the environment, health** and **disease**.



Research Nurse, Barbara Graves, with one of our volunteers

- Joining the volunteer panel requires a one-off appointment at the research unit (located on the Addenbrooke's campus), and collection of a blood or saliva sample.
- Volunteers are then 'matched' to research studies and invited to take part.
- Participation in any study is voluntary, and the team work with volunteers to find a convenient time/location.
- Recruiting volunteers aged 16+





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The Participants



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