Hope for the future

RTCure
Rheuma Tolerance for Cure

Changing the treatment paradigm from late treatment towards prevention and very early treatment

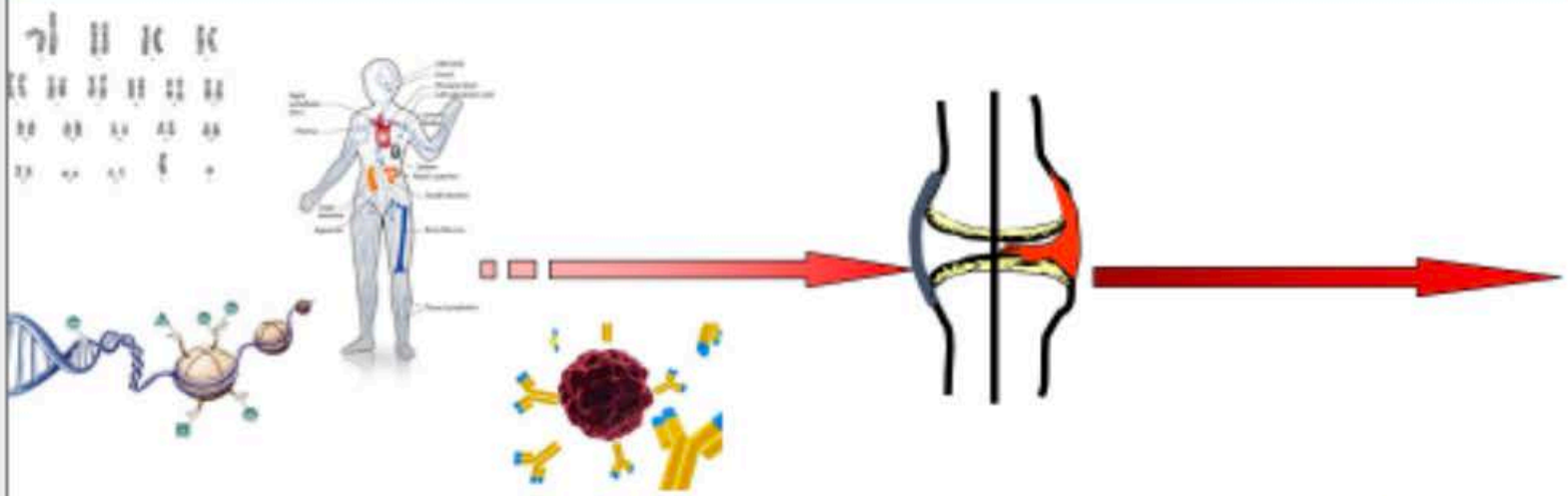
RTCure
Rheuma Tolerance for Cure

With new solutions:

- Early detection
- Patient driven prevention
- E-health driven coordination
- Aiming for prevention and cure
- Collaborative and iterative process

Needed ← Current

Genes, vironment | Immune system activation | Immune attack | **Inflammation** | Tissue destruction Organ failure



No signs and symptoms | Unspecific symptoms | Disease diagnosis | Disability

At risk for inflammation | Pre-Disease Symptoms and biomarkers | Early Disease | Disease

Today:
Late disease detection and unspecific treatment options

Too little patient involvement

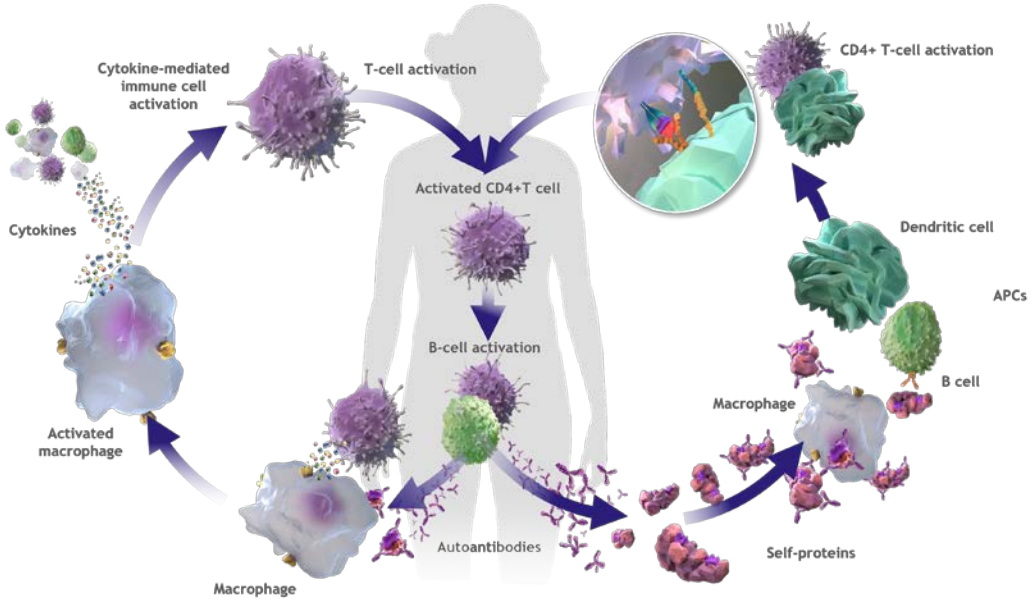
No cures - symptomatic relief and bad long-term outcomes

Current therapies associated with many side-effects

Major healthcare concern and health economic burden

Standardising experimental methods across multiple labs

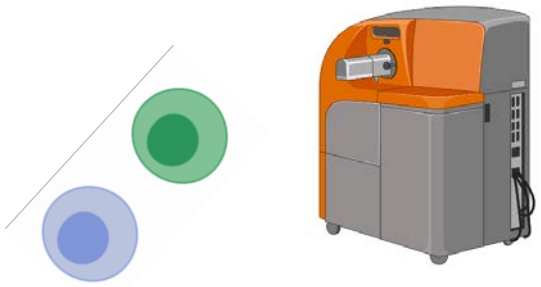
Many cells make up the immune system and could be contributing to inflammation in RA.



Question: How can we monitor changes in these immune cells due to treatment?

Analysing cells in blood gives us clues

Flow cytometry and mass cytometry



Multiple labs successfully followed the same protocols to enable comparisons of data more reliably

- Hundreds of samples
- Millions of cells
- 40+ parameters
- Lots of questions

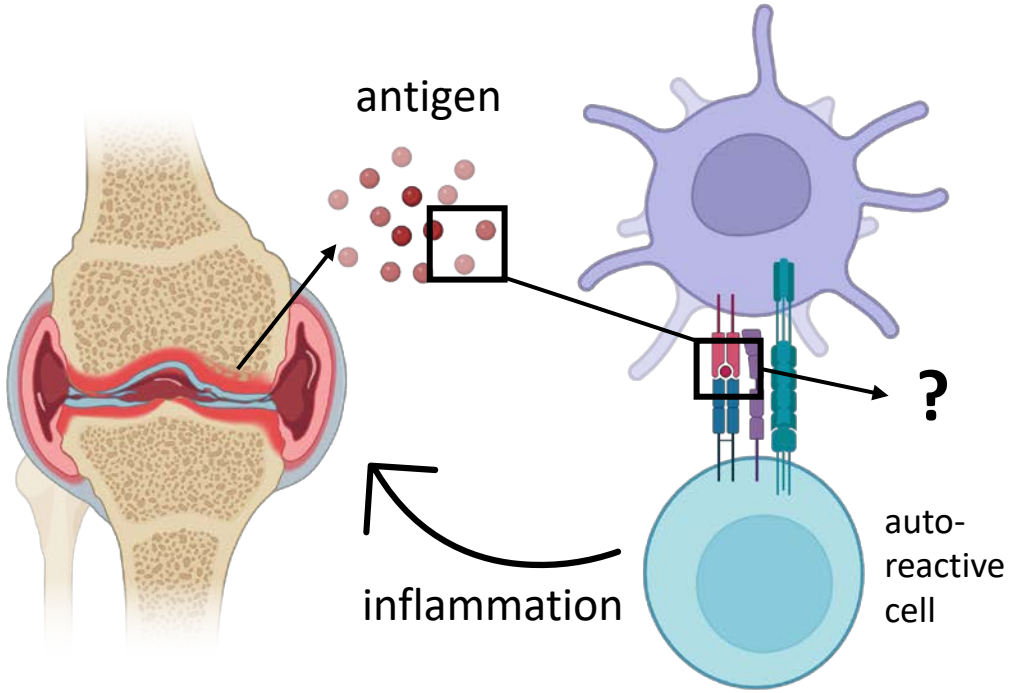
➔ **WHAT NOW?!?**

COMPUTERS!

Establishing new understanding of antigen-specific T and B cells

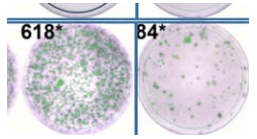
Question

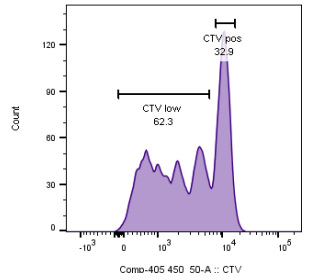
Which antigen-specific immune reactions are present in RA patients and how do their numbers and phenotypes change due to use of different therapies.



Progress

RTCure has made major progress in establishing assays that can measure antigen specific immune reactions in RA

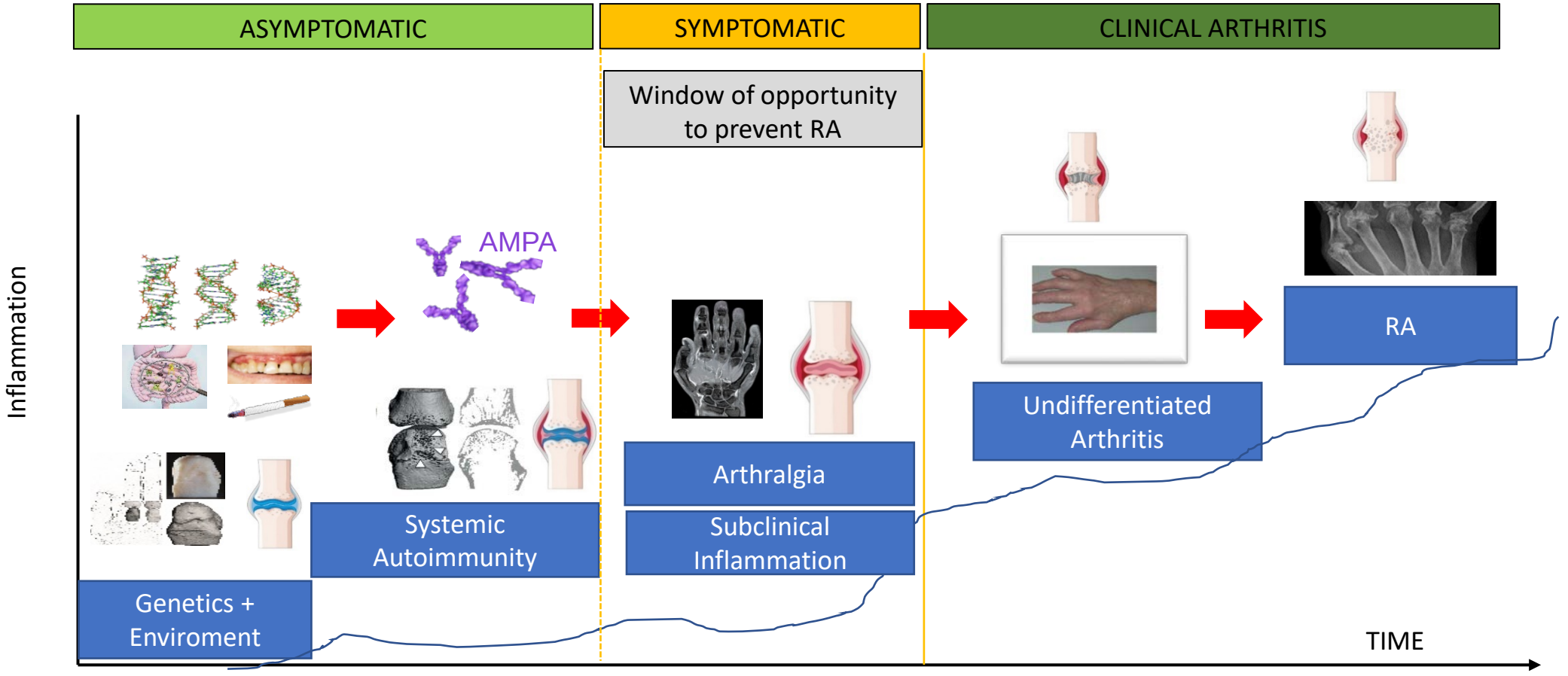




Learnings

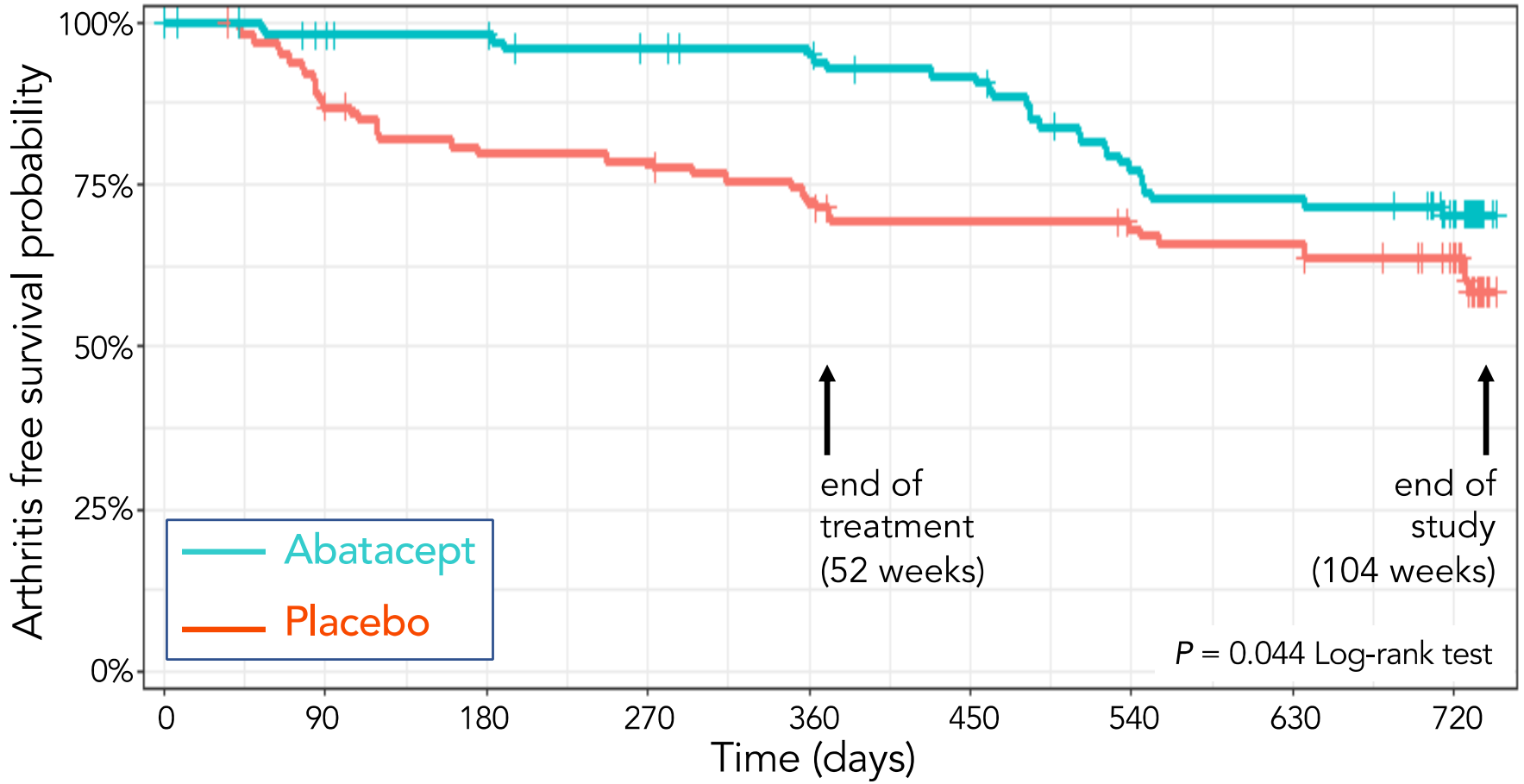
- Many antigens to chose from; each lab has its favourites!
- Multiple readouts; even with harmonization the results can vary a lot
- Low precursor frequency remains a challenge
- Patient specific signatures are typical
- And many more….

Autoimmunity and pain precede develoment of RA; This provides an opportunity for prevention



Slide from John Isaacs, Newcastle

Arthritis-free survival in the APIPPRA trial



Trial funded by Bristol Myers Squibb

N=213

ITT analysis

Impact of IMP on symptom burden

APIPPRA
Arthritis Prevention In The Pre-Clinical Phase Of RA With Abatacept

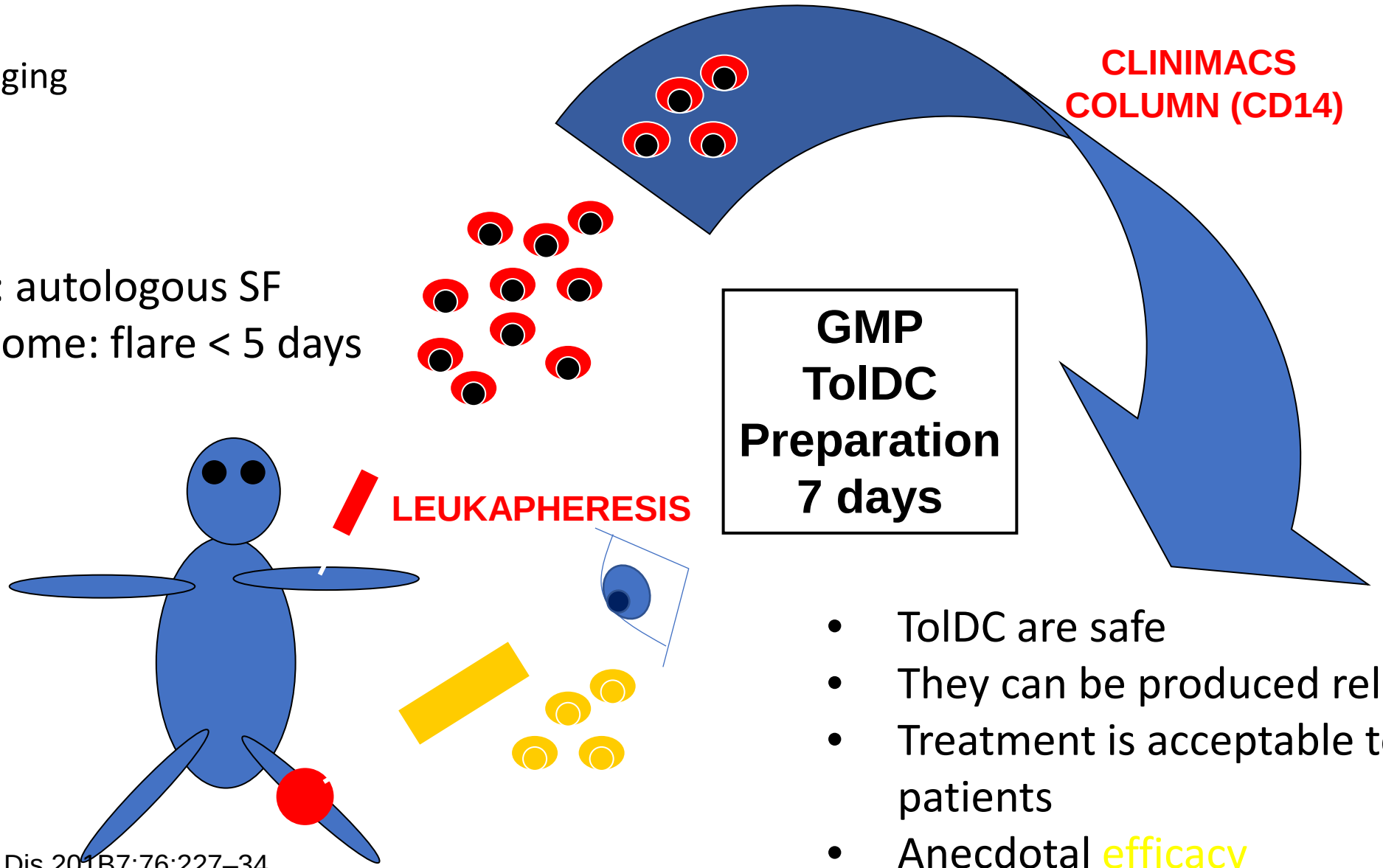
During the treatment phase, and when compared to placebo, abatacept also:

- Reduced fatigue (FACIT-F)
- Improved physical and emotional wellbeing (FACIT-F)
- Improved functional wellbeing (FACIT-F)
- Reduced sleep problems (SPARRA)
- Reduced levels of anxiety (HADS-A)
- Positive impact on work instability (RA-WIS)
- Positive impact on illness beliefs (IPQ-RA)

Towards tolerance: Autologous Tolerogenic Dendritic Cells for RA (AUTODECRA) (John Isaacs, Cat Hilkens et al, Newcastle)

Dose-ranging
Phase 1
Safety

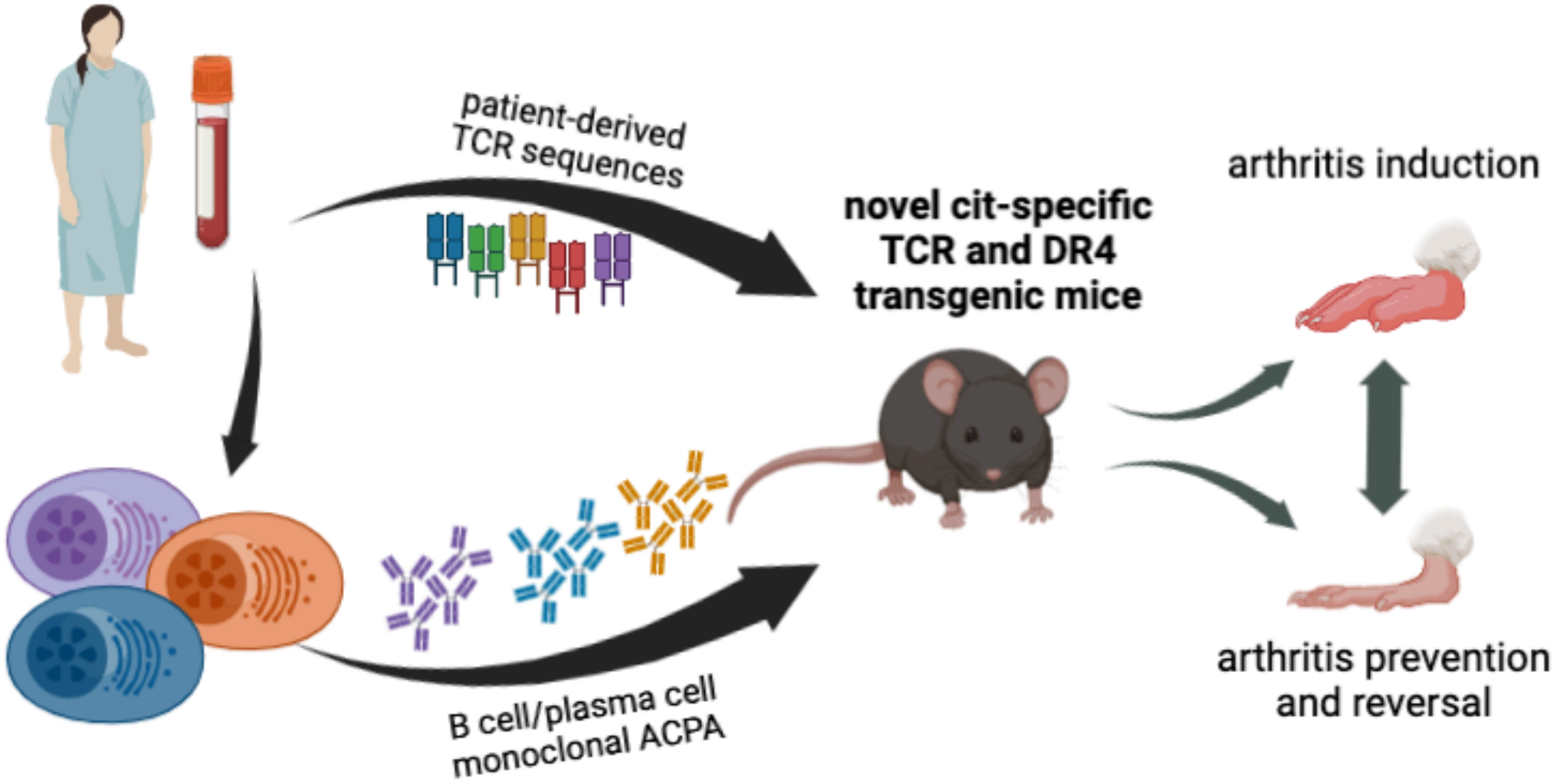
Autoantigen: autologous SF
Primary outcome: flare < 5 days



- TolDC are safe
- They can be produced reliably
- Treatment is acceptable to patients
- Anecdotal efficacy

Ann Rheum Dis 201B7;76:227–34

Our ambition:
Use mice with human immune components for development of the next generation of tolerance therapies



Slide from Bruno Raposo

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