

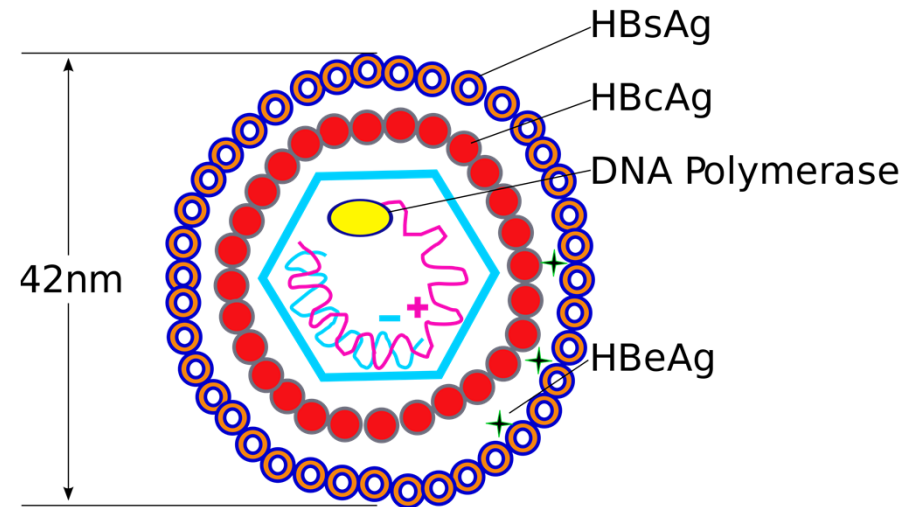
How Hepatitis B vaccine response and non-response can immunologically be explained

Pieter Meysman

25 April 2019

Hepatitis B vaccine

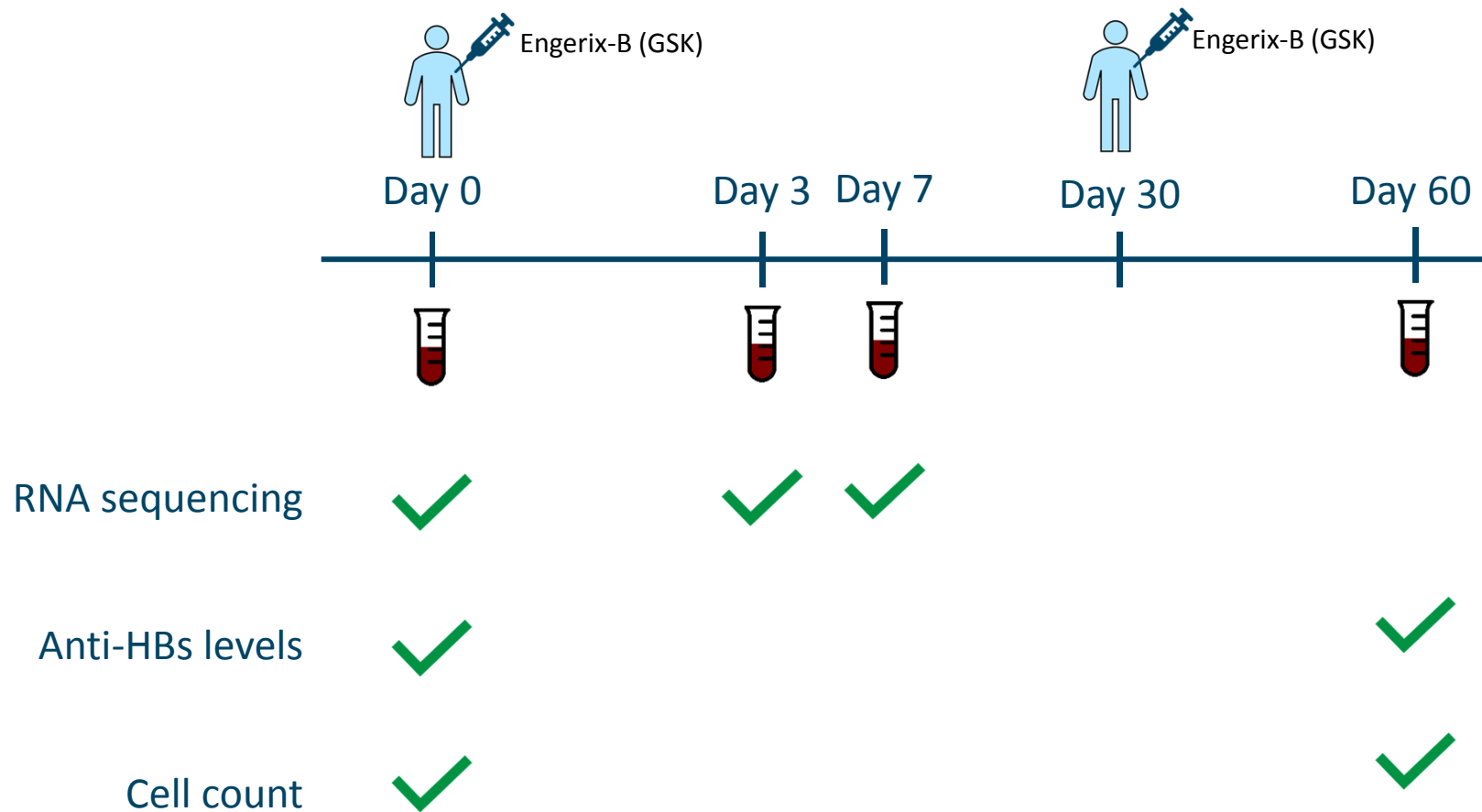
- Uses Hepatitis B surface antigen (HBsAg)
- 3- to 4-dose vaccination scheme
- 5%-10% non-responders
- Life-long protection



Source: Wikimedia commons

Experimental overview

- Recruited 33 individuals with no prior Hepatitis B vaccination or disease history.

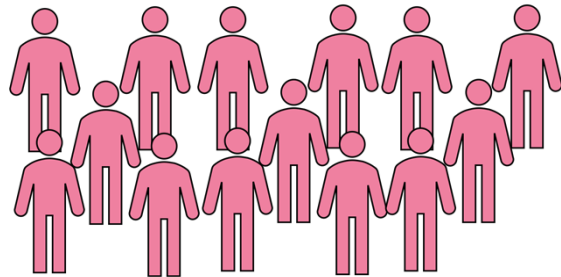


Ref: Bartholomeus et al. Vaccine. 2018

Response at day 60

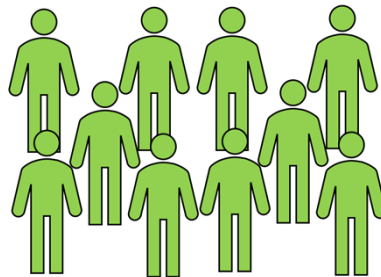
42% non-responders after two doses

14 Non-responders



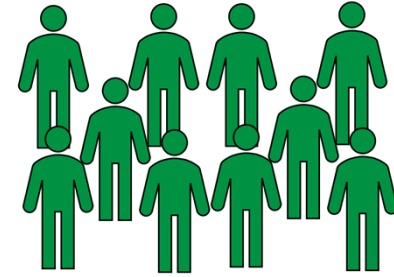
Ab titer < 10 mIU/ml

10 Low responders



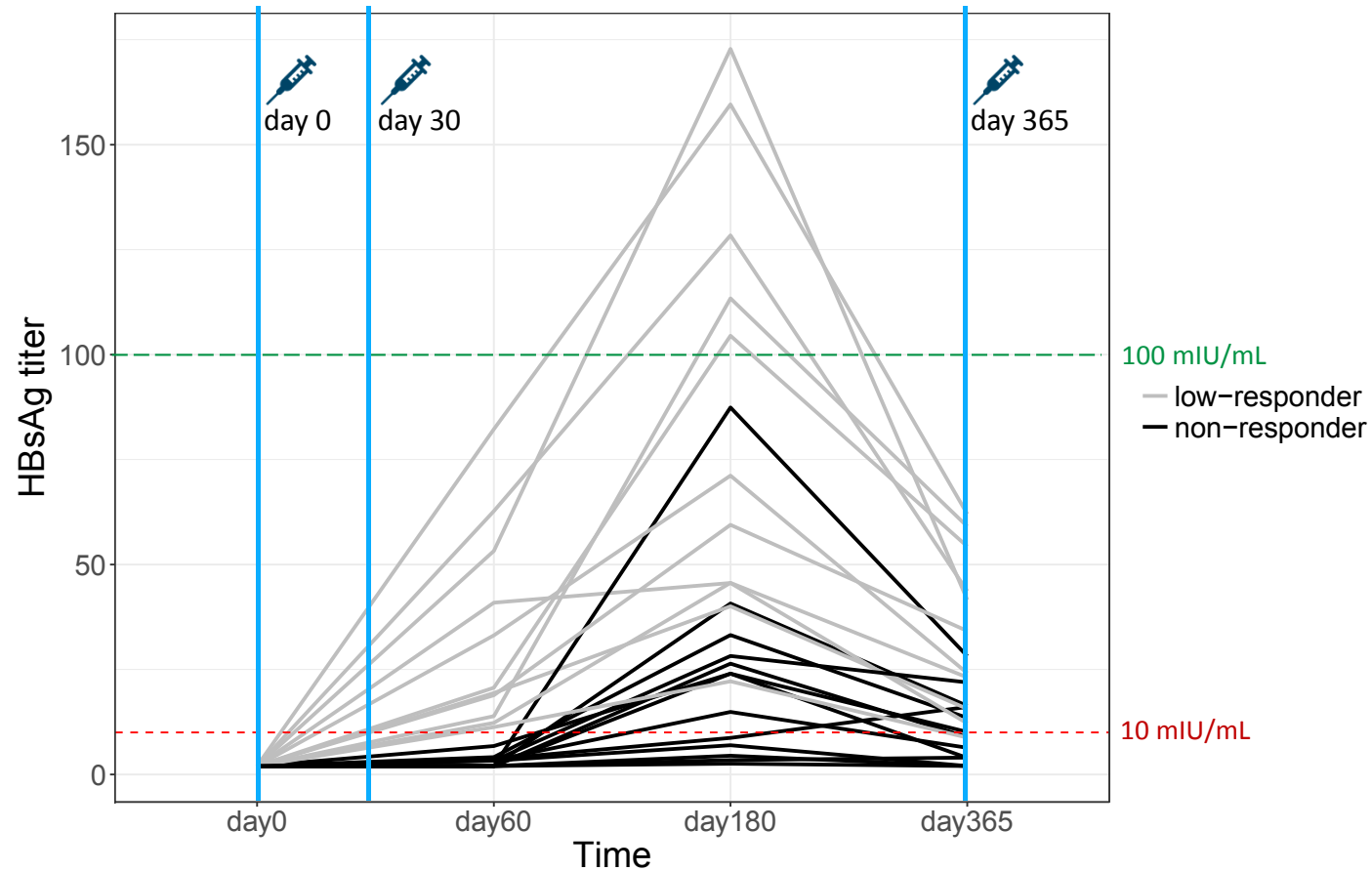
10 < Ab titer < 100 mIU/ml

10 Strong responders



Ab titer > 100 mIU/ml

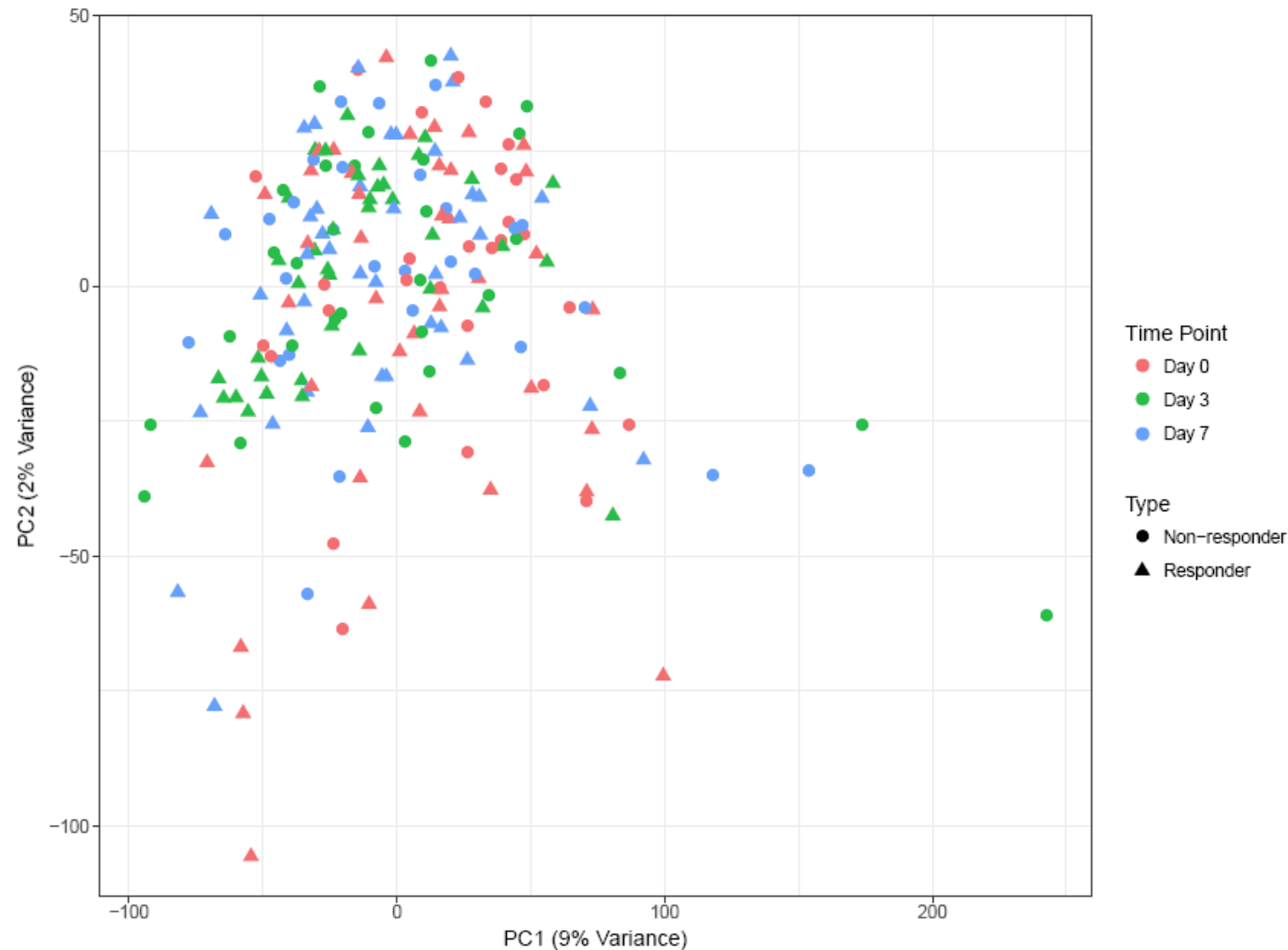
Progression of response



- Most of the non-responders at day 60 do increase later

RNA sequencing: PCA analysis

Largest source of variation is individual specific



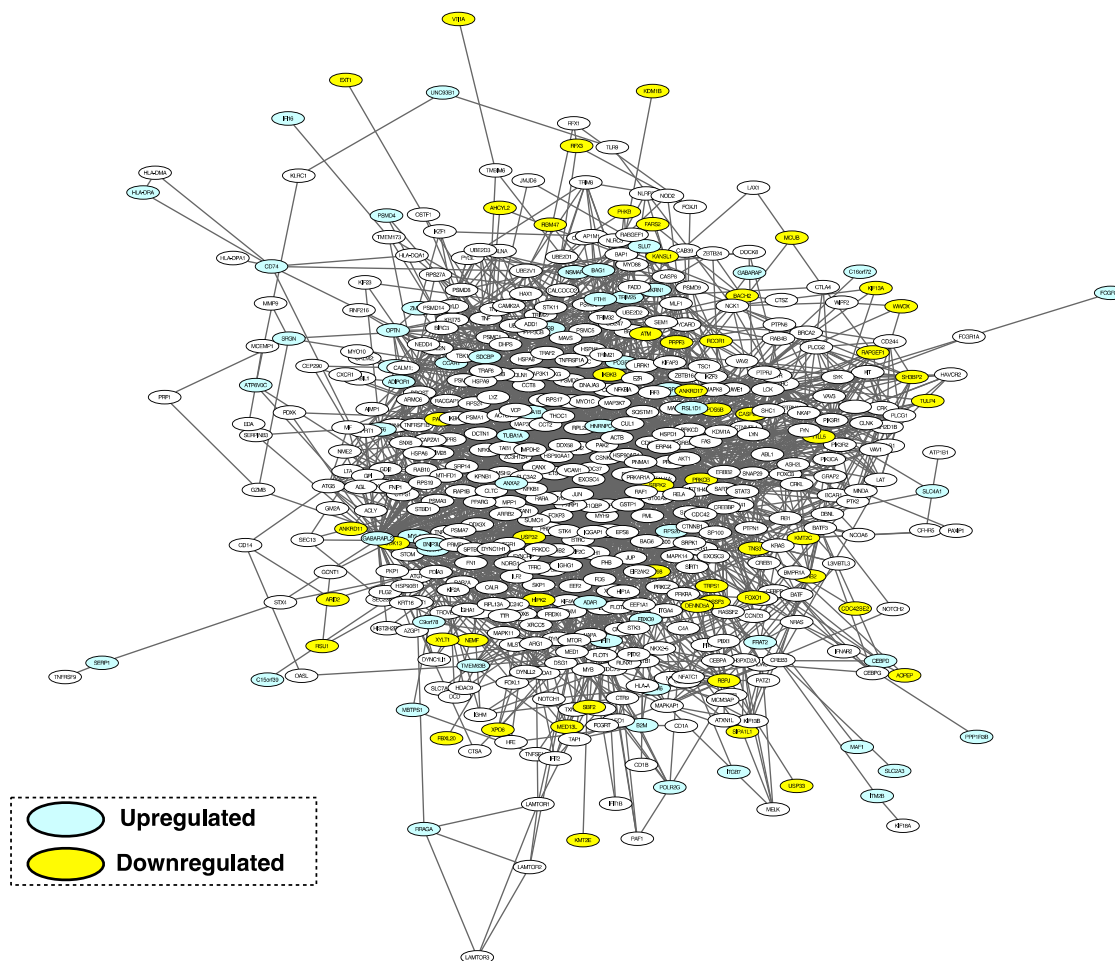
RNA sequencing

How does the gene expression change in response to the vaccine?

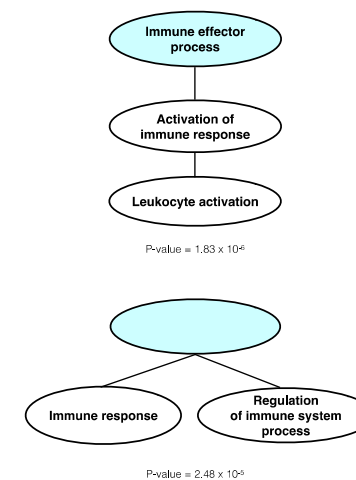
Resulting differential expressed genes (DEGs):

Dataset / #DEGs	Day 3 vs Day 0	Day 7 vs Day 0
Responders	349	40
Non-responders	10	155

Many DEGs associated with the immune system

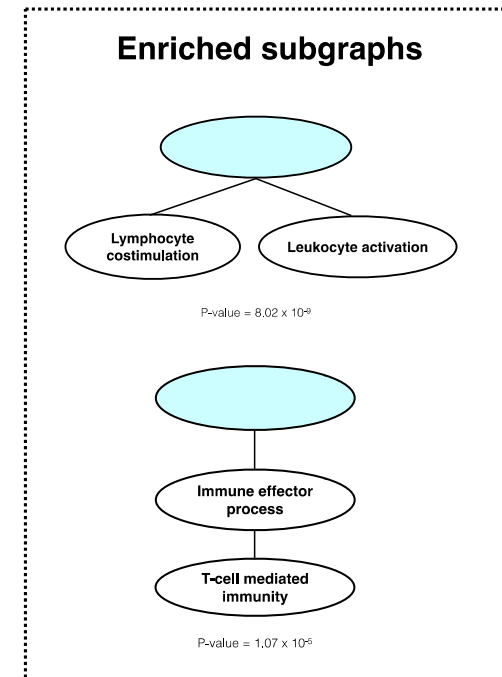
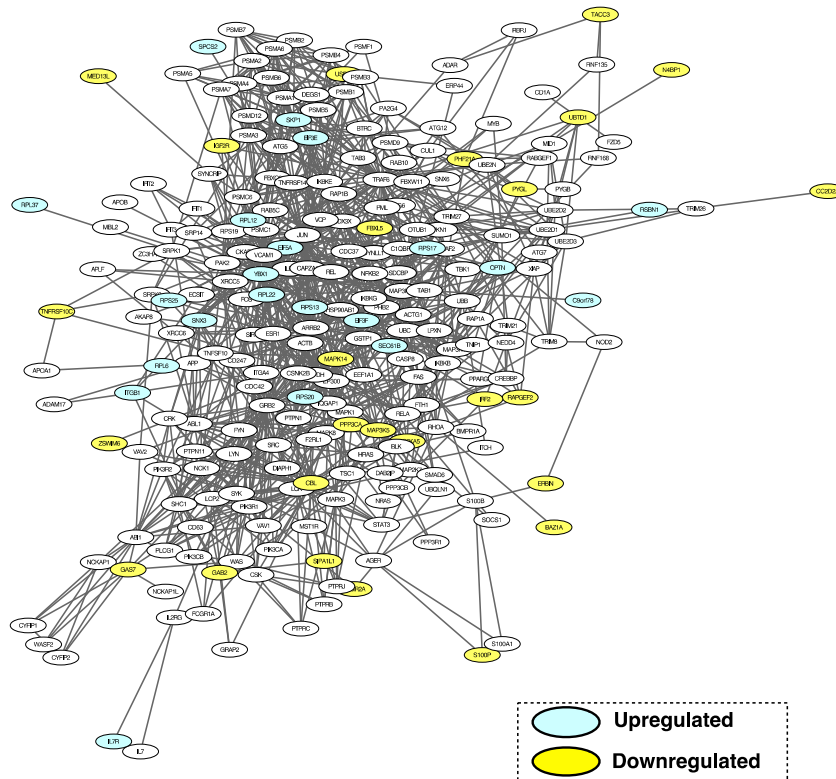


Enriched subgraphs



Ref: Meysman et al. IEEE TCBB. 2016

Non-responder | Day 7 vs Day 0 | PP network



Ref: Meysman et al. IEEE TCBB. 2016

- ✓ Upregulation of T-cell mediated immunity, leukocyte activation and lymphocyte costimulation

RNA sequencing

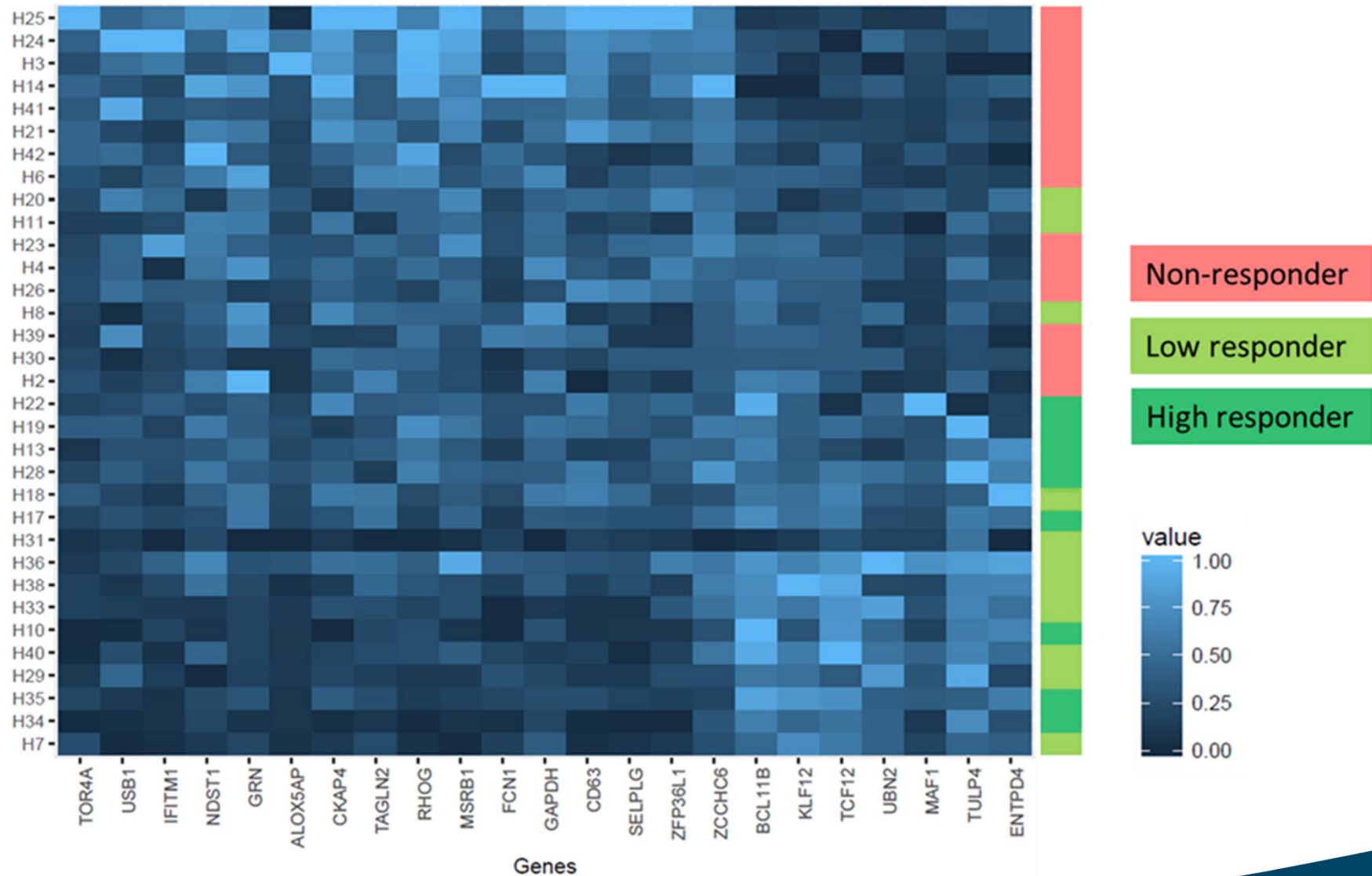
How does the gene expression differ between responders and non-responders?

Resulting differential expressed genes (DEGs):

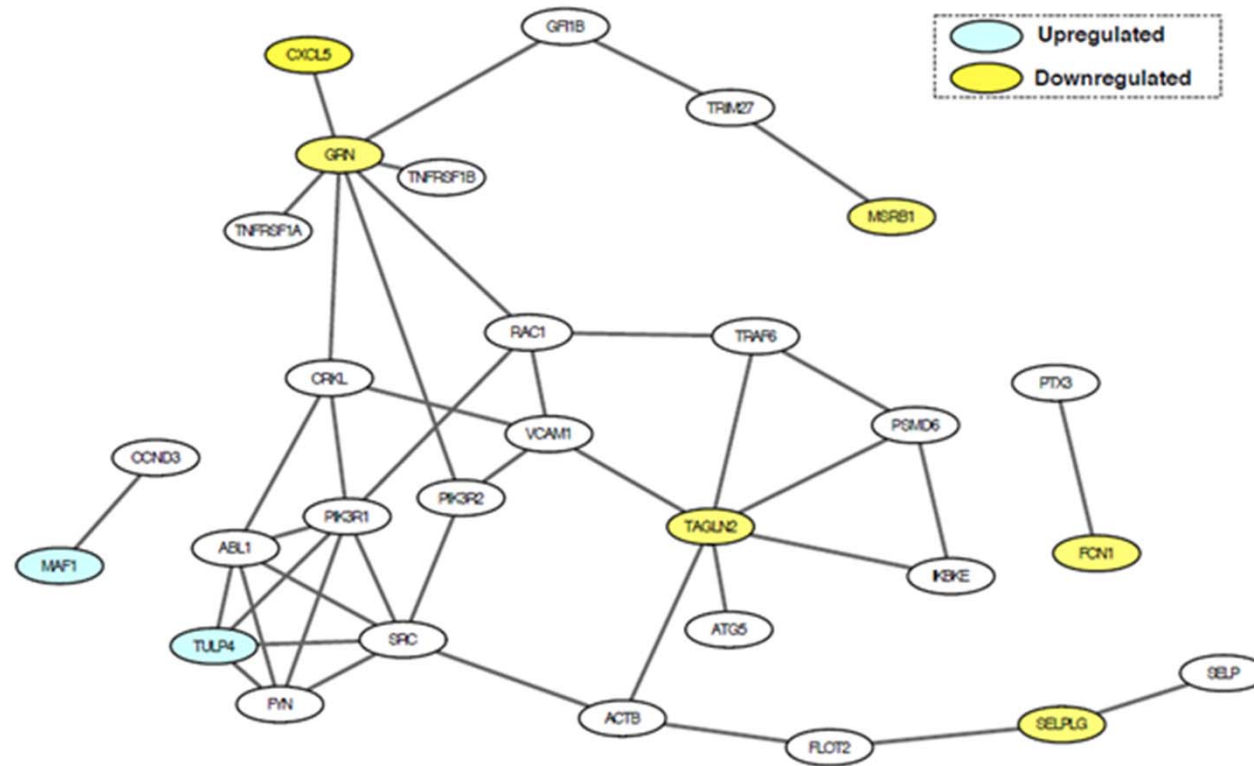
Dataset / #DEGs	Day 0	Day 3	Day 7
Responders vs Non-responders on each time point	23	9	0

Biggest difference on day 0 (before the vaccination)

Time point | Day 0 | Expression profile

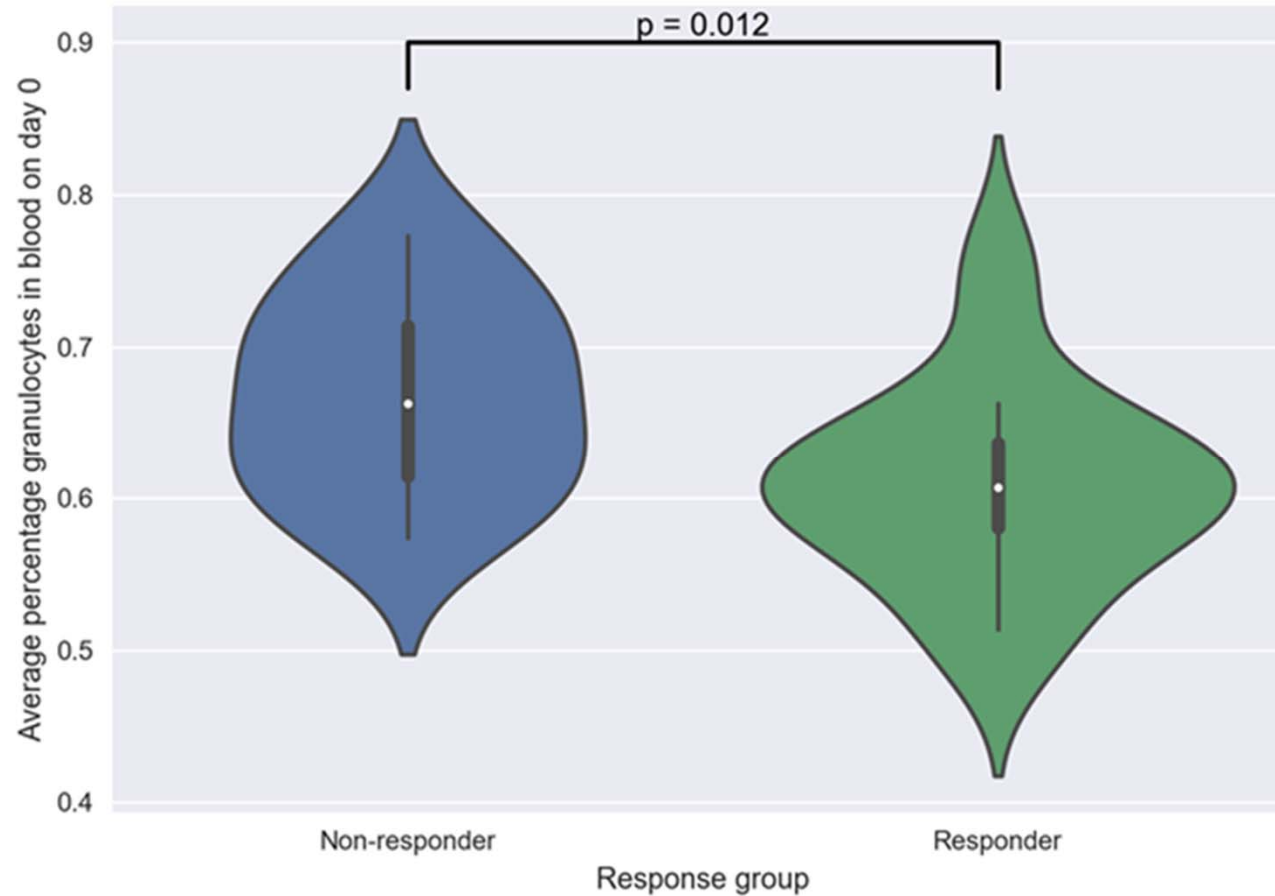


Time point | Day 0 | Protein-protein network



- ✓ Granulin (GRN), cell growth regulator
- ✓ CXCL5, cytokine
- Role in inflammation and host immune defense

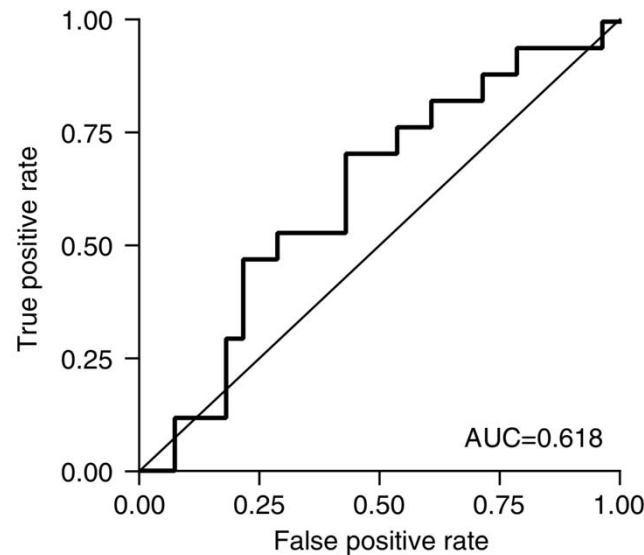
Time point | Day 0 | Granulocytes



- ✓ Granulin is secreted by granulocytes

Predictability of vaccine response

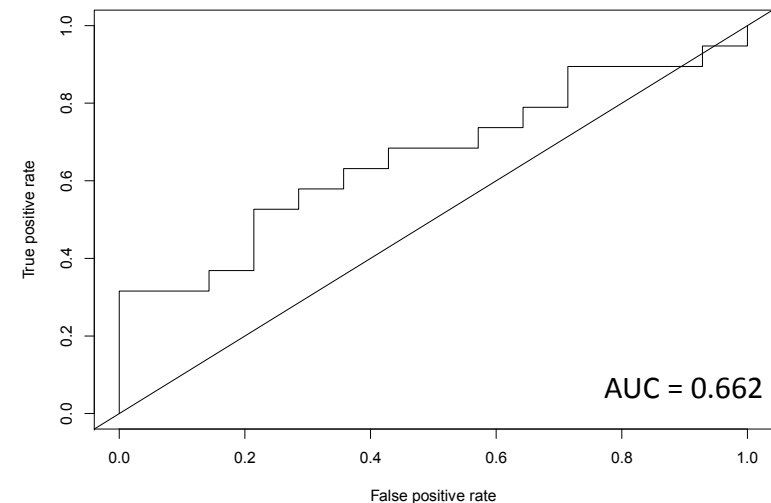
- Use of gene expression data before vaccination to predict long term response.



Micro-array (n=174)

15 gene probes

Ref: Fourati et al. Nature Comm. 2016



RNAseq (n=33)

10 principal components

Ref: Bartholomeus et al. Vaccine. 2018

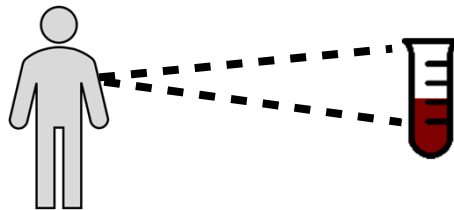
Take home message

- Inter-variability of individuals
- Immune peak response:
shift between responder and non-responders
- Day 0 differences
- The role of granulocytes and secretion of granulin
- Gene expression-based classifier not yet good enough
for clinical practice

Acknowledgements

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- Prof. Benson Ogunjimi
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Next-generation sequencing

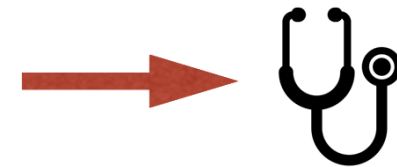
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- drs Esther Bartholomeus



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