



PLN onderzoek

Behandelingsmogelijkheden

Luuk Kerckhaert

Derdejaars geneeskundestudent

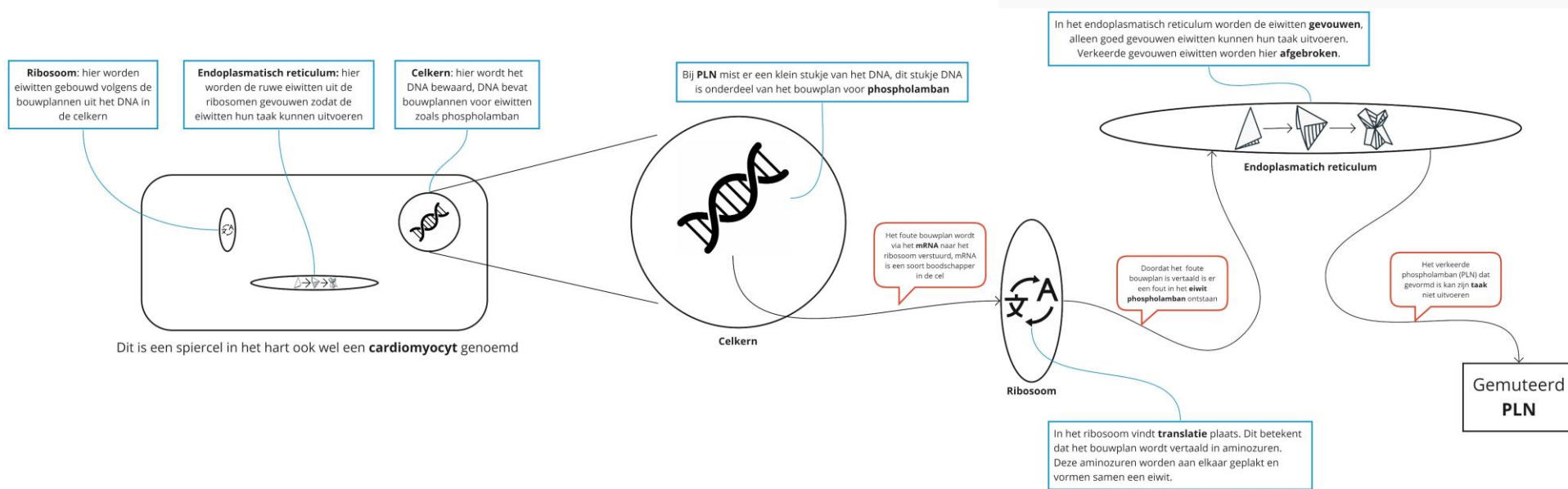
Wetenschappelijk adviseur Stichting PLN

PLN Webinar 2021

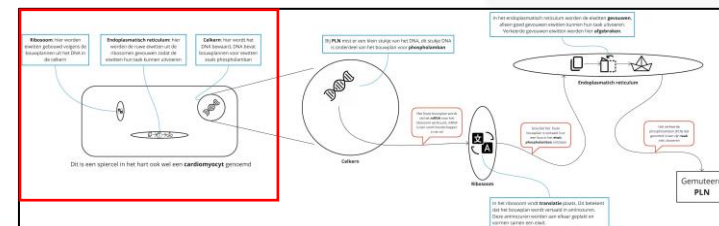
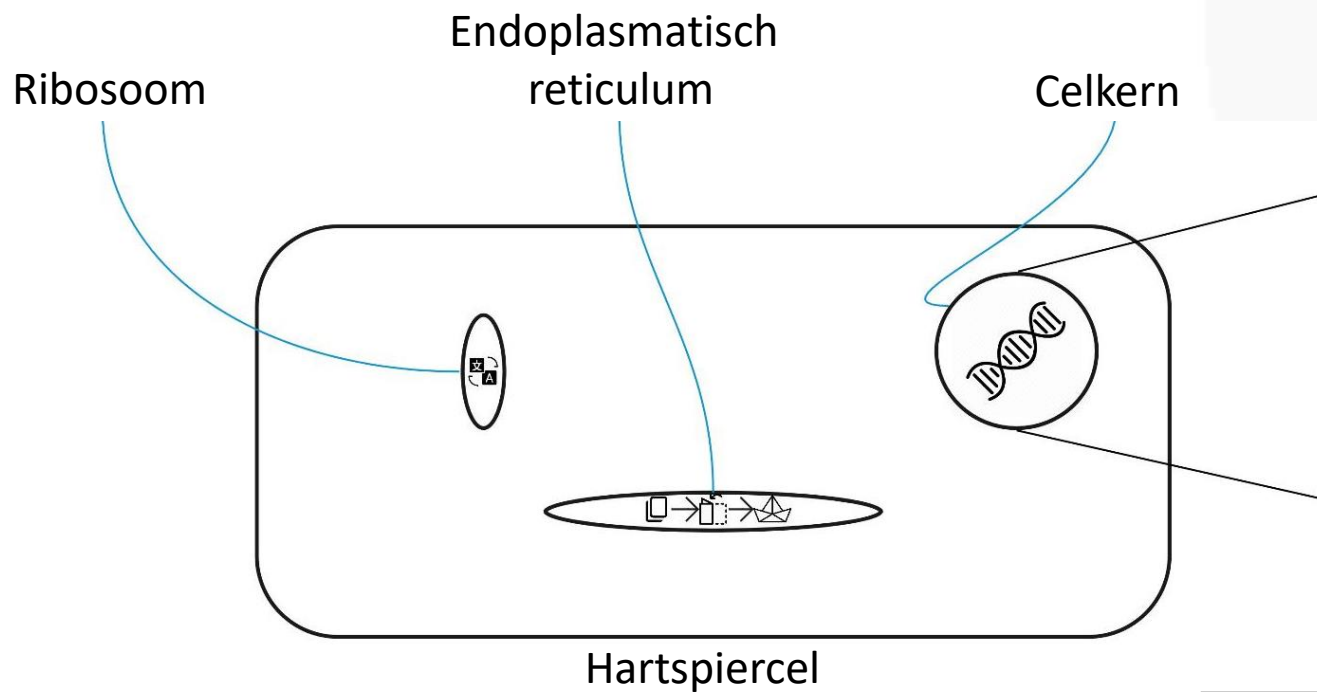
Inhoud

- Vorig jaar
- Behandelingsmogelijkheden
 - Calcium 'opruimers'
 - DWORF
 - Antilichamen
 - Aptameren
 - Antisense RNA
- Conclusie

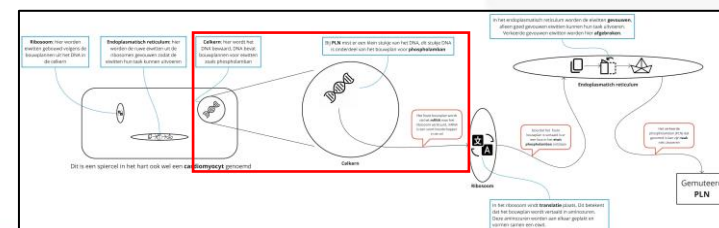
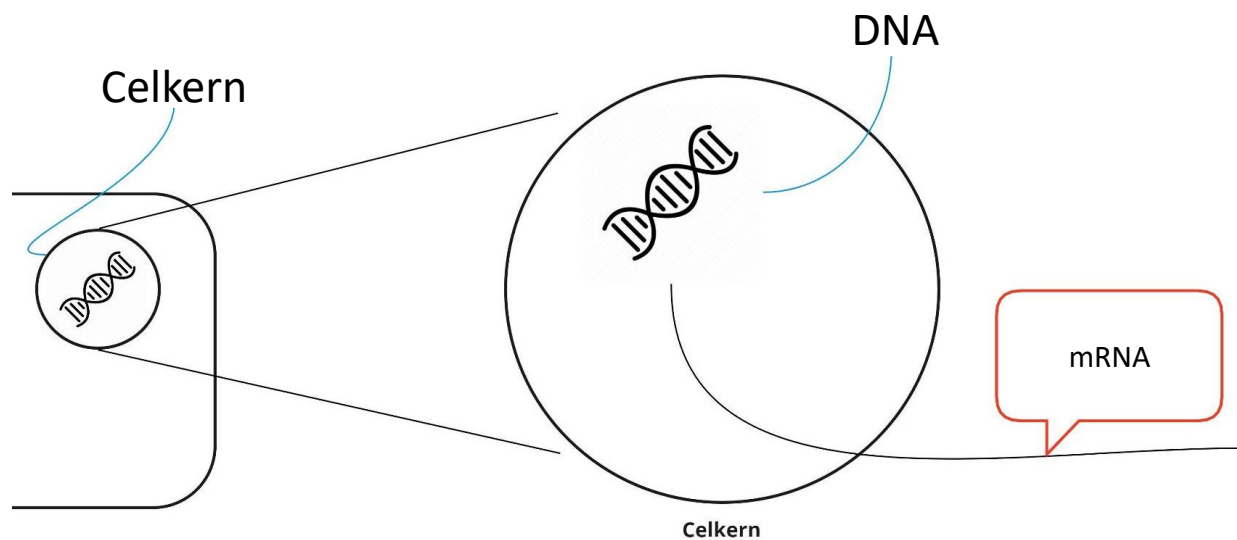
Vorig jaar: productie PLN



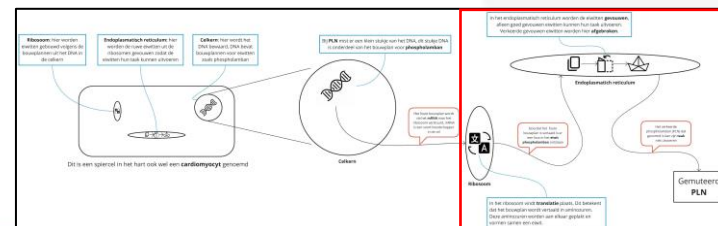
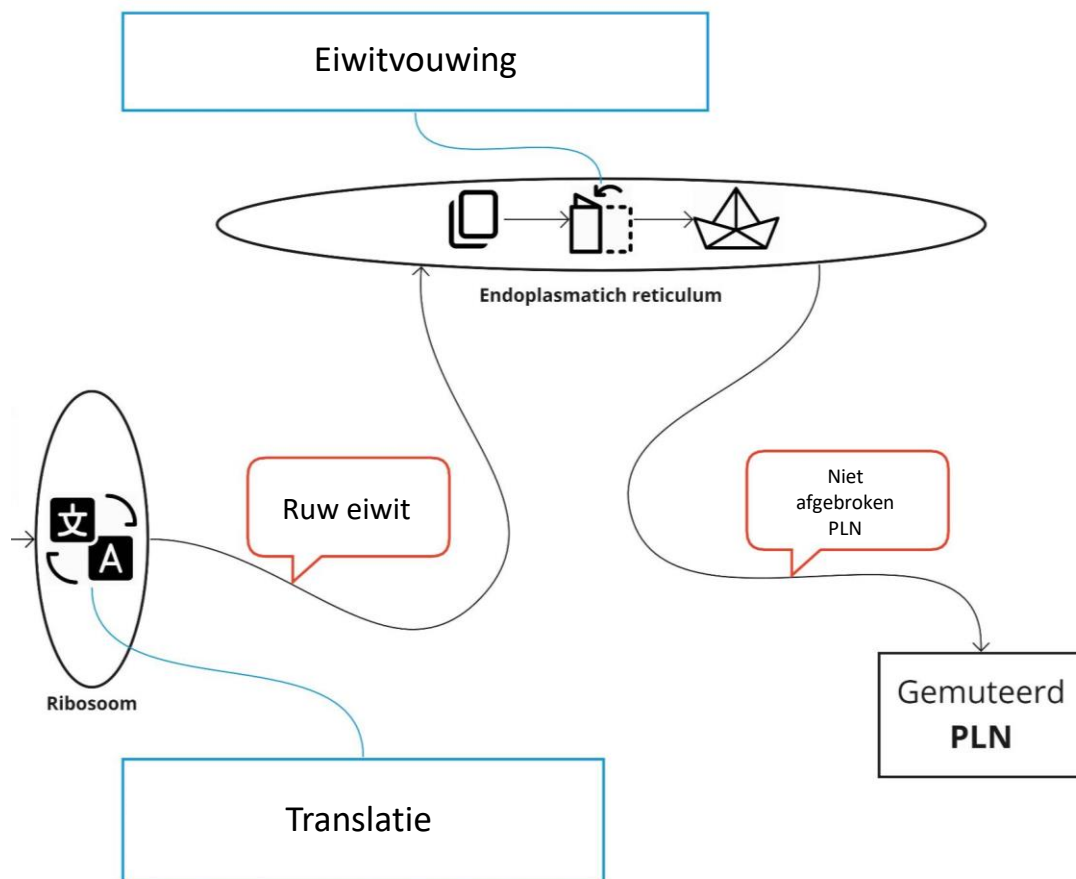
De hartspiercel



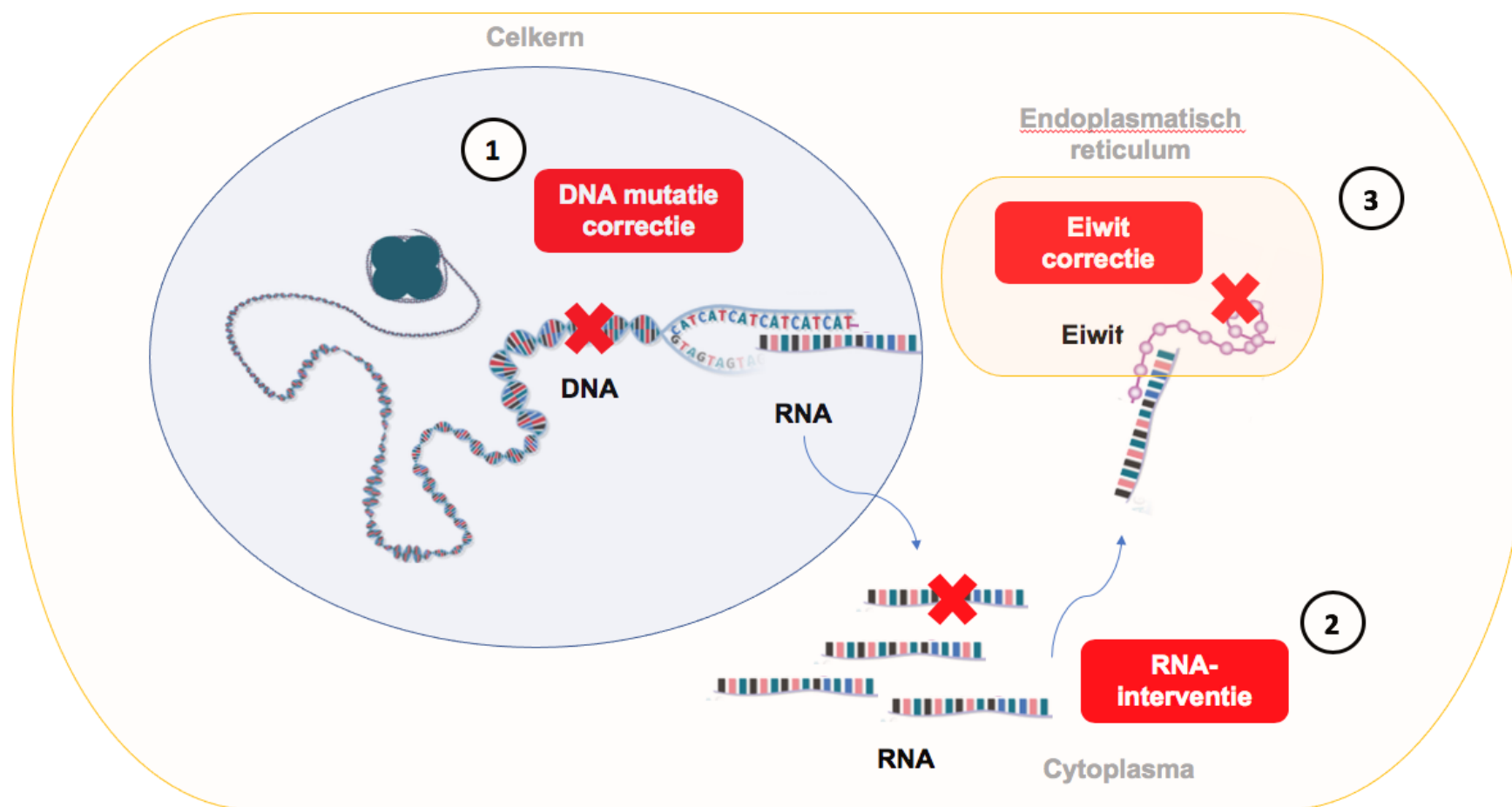
De celkern



De ribosomen en het endoplasmatisch reticulum



Behandelingsmogelijkheden



Adapted from: <https://www.garvan.org.au/research/kinghorn-centre-for-clinical-genomics/learn-about-genomics/dna-base/collection1/dna-chromosomes-and-cells>

Behandelingsmogelijkheden

- Bestaande medicijnen

- Eplerenon and metoprolol
- Metformine
- Istaroxime



- RNA 'afvangen'

- Short interfering RNA (siRNA)
- Short hairpin RNA (shRNA)
- Antisense RNA (asRNA)



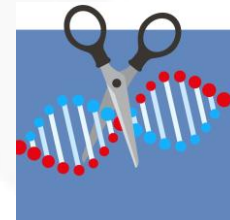
- Kleine moleculen

- BiP protein inducer X (BIX)



- Gen therapie

- Crispr-CAS
- Prime editing



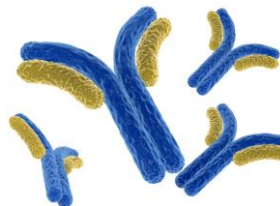
- Peptides

- DWORF
- 14-3-3
- Calcium 'opruimers'

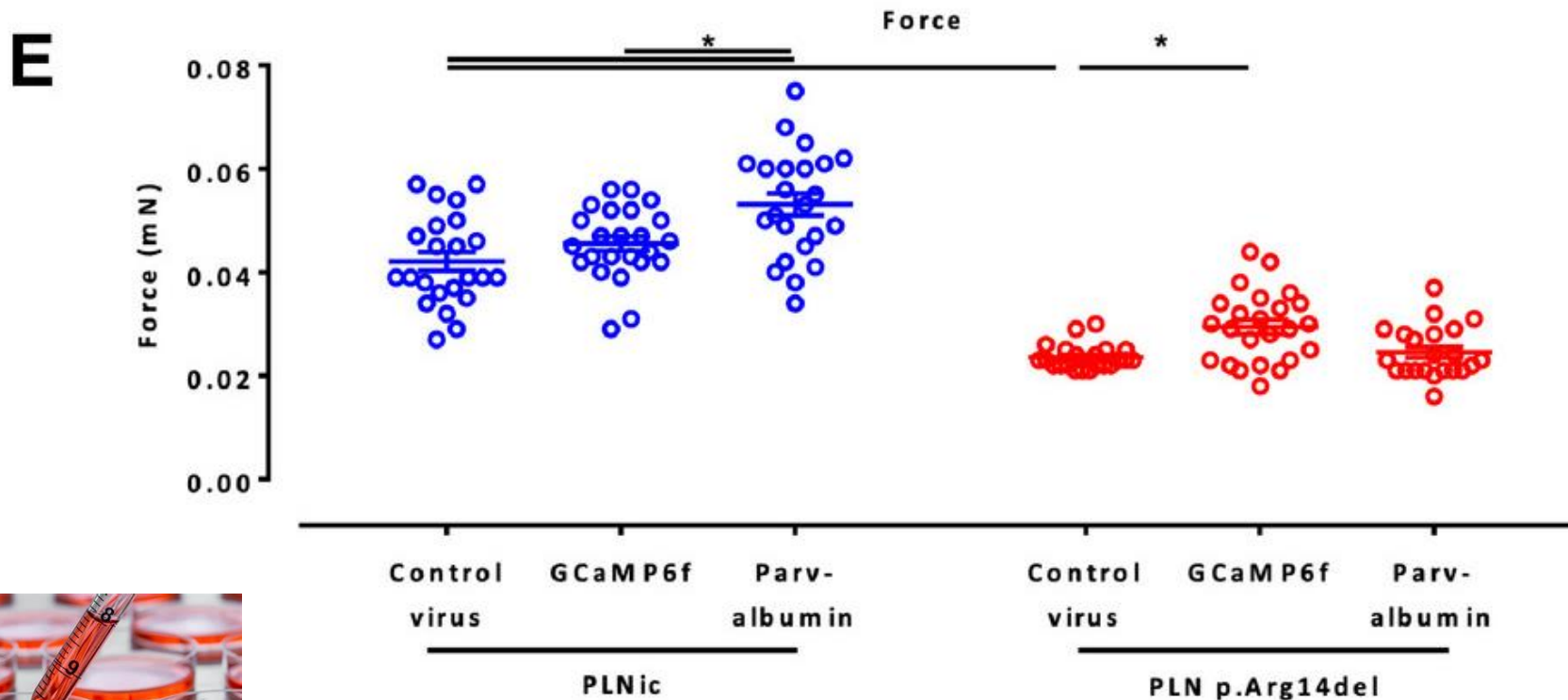


- Gerichte therapie

- Aptameren
- Antilichamen (antistoffen)
- Nanobodies (mini antilichamen)



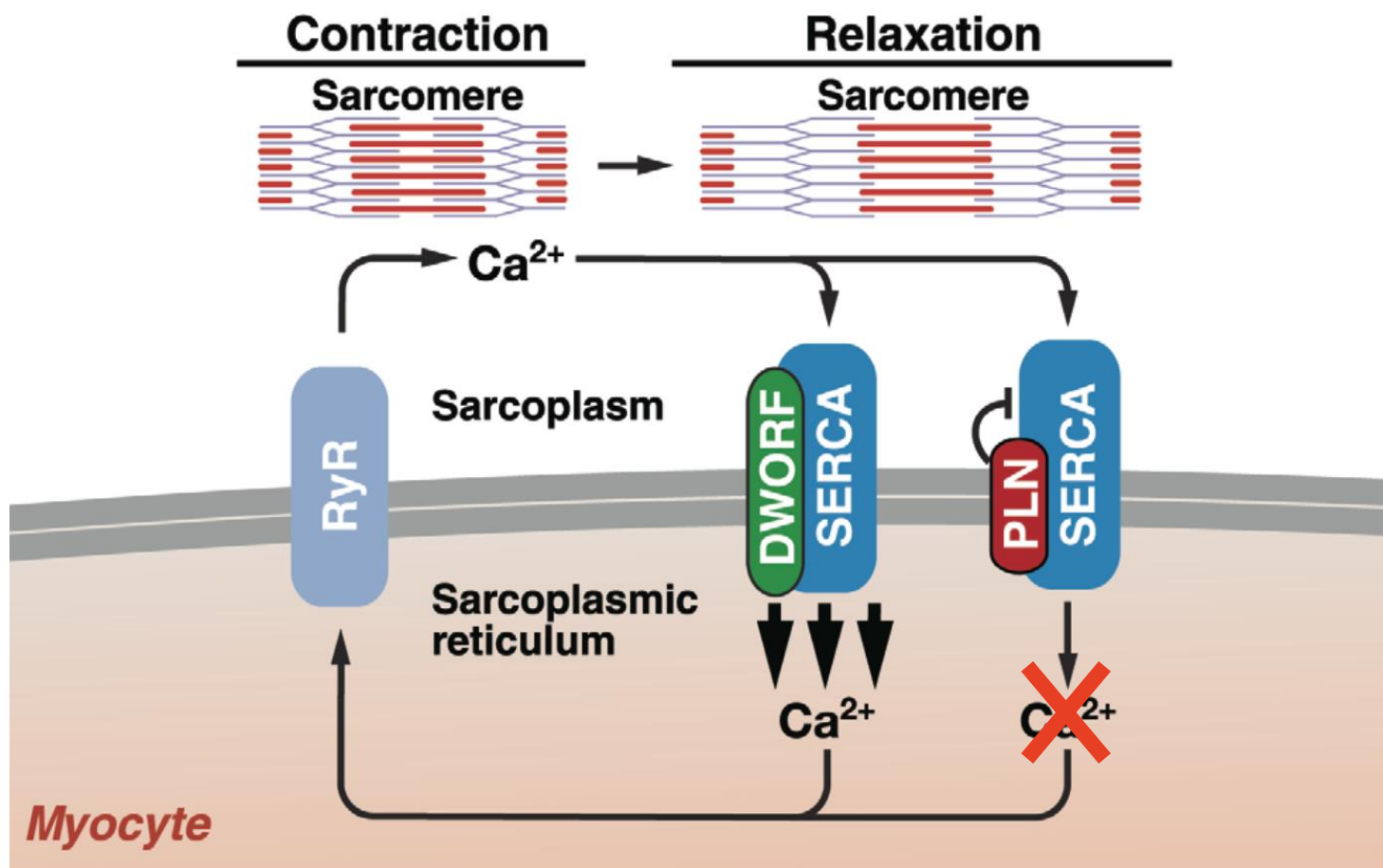
Calcium 'opruimers'



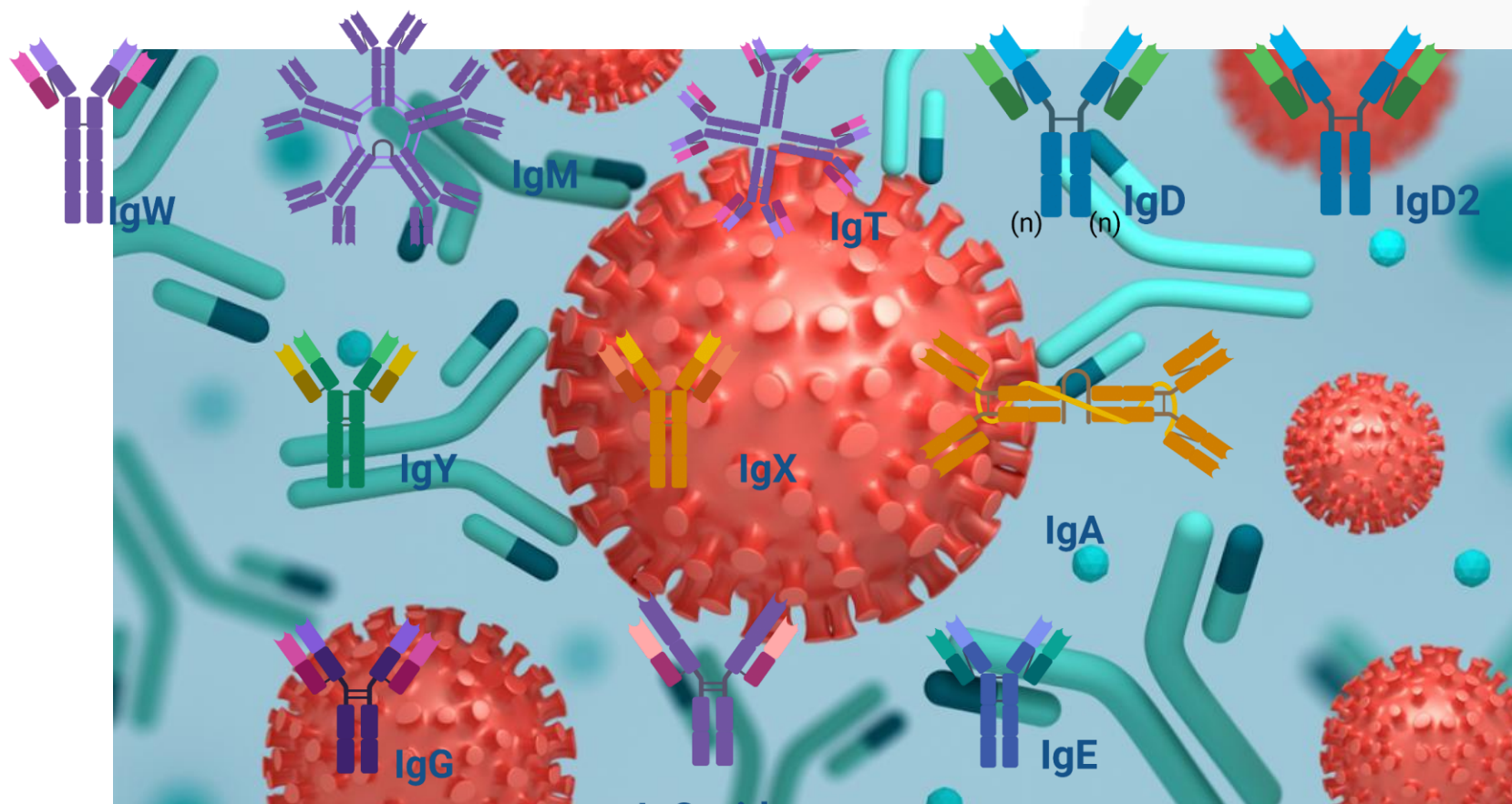
Human induced pluripotent stem cell derived **cardiomyocytes**

Cuello, 2021

DWORF

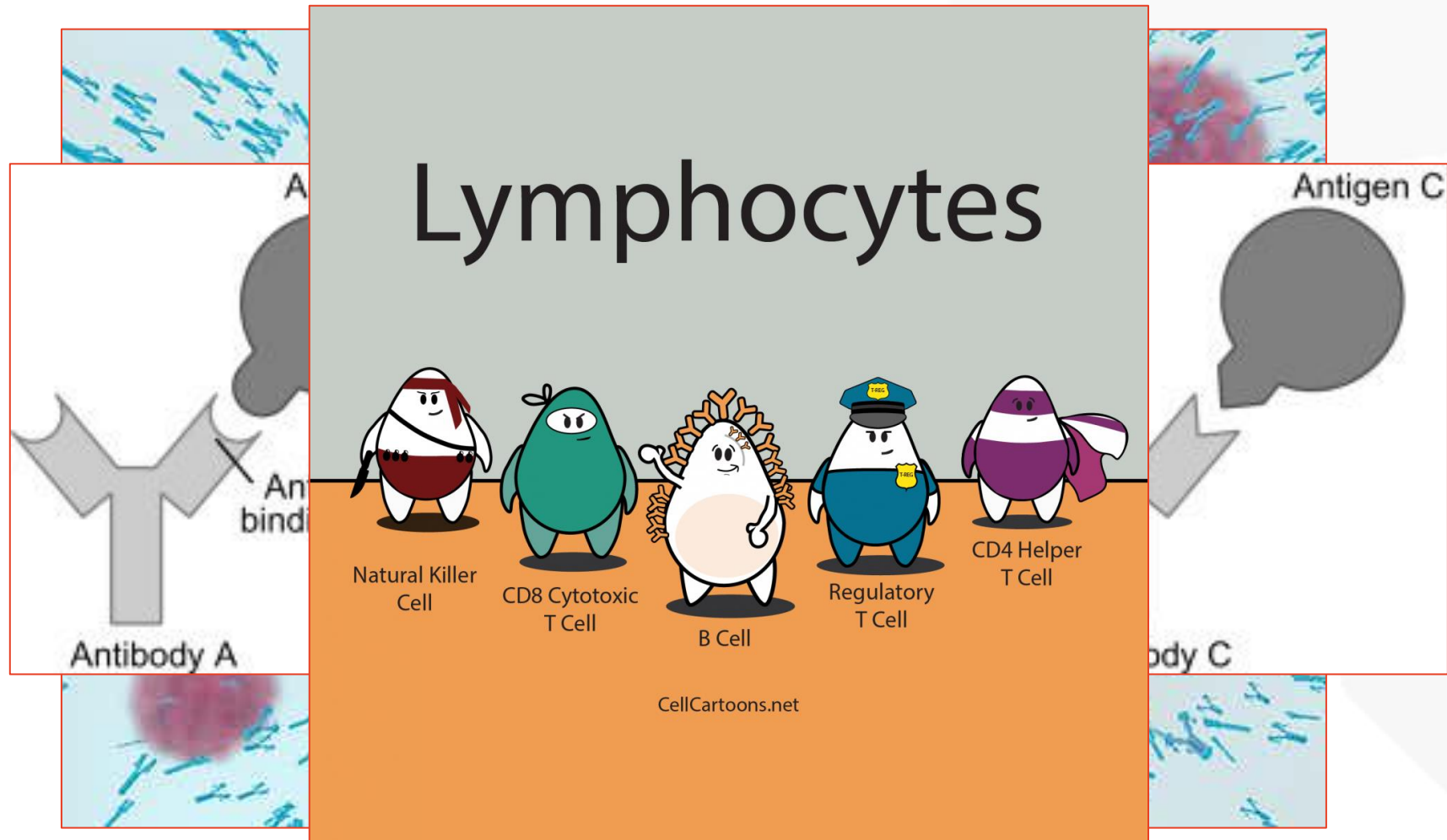


Antilichamen

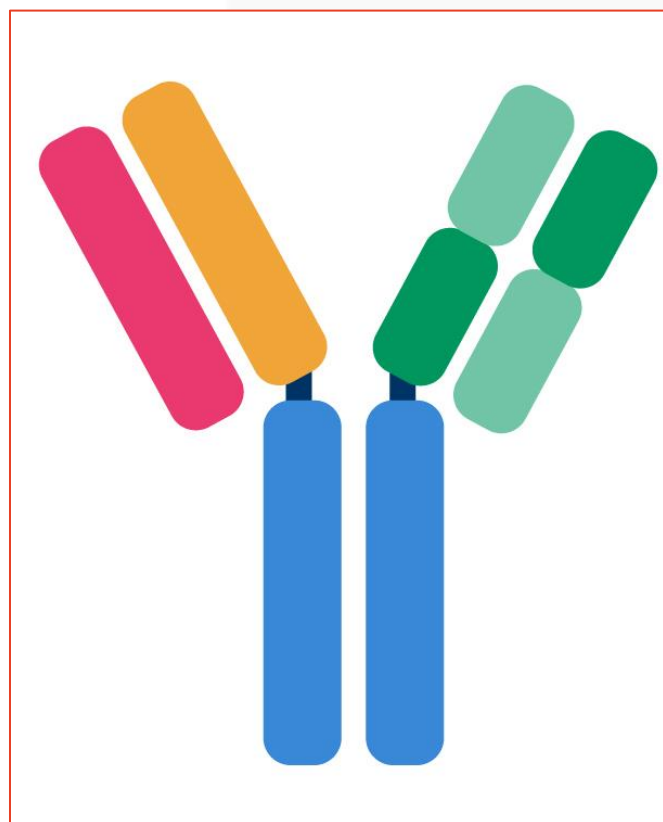
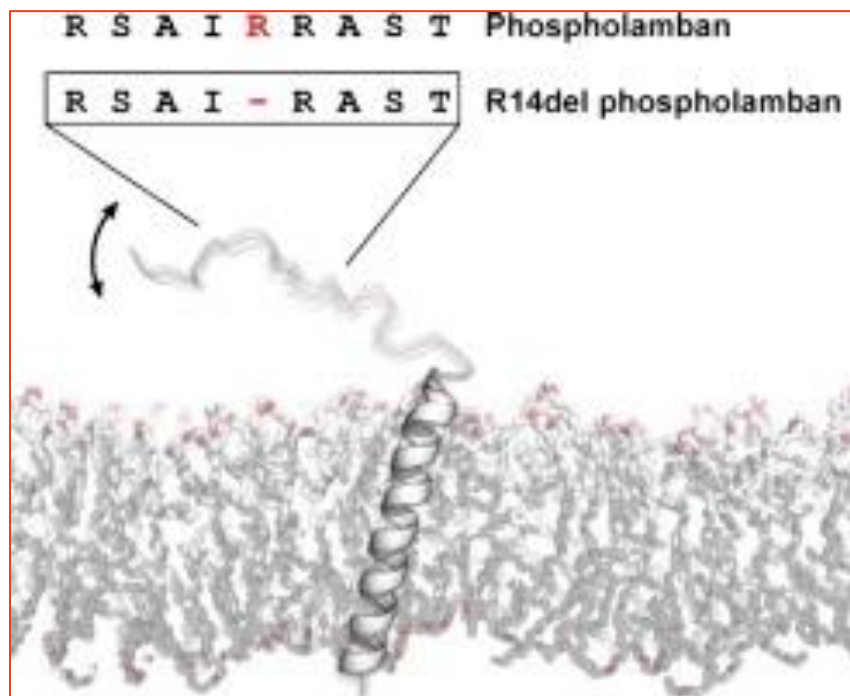


**IgG with
ultralong CDR H3**

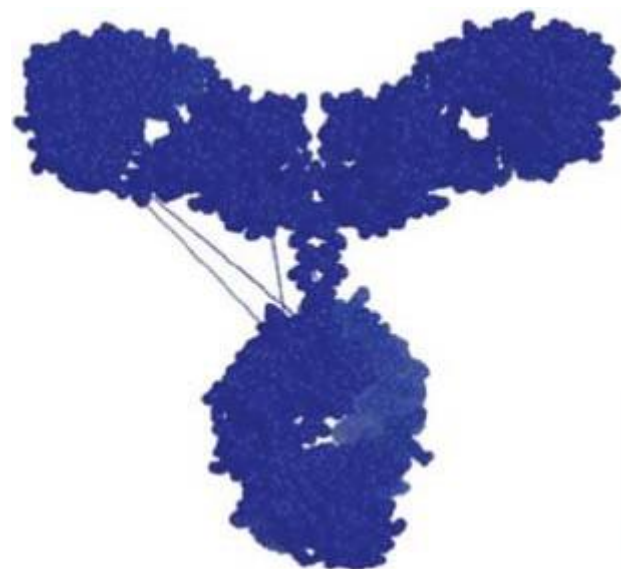
Uitstapje: antilichamen en virusinfectie



PLN en antilichamen



Aptameren



Antilichaam

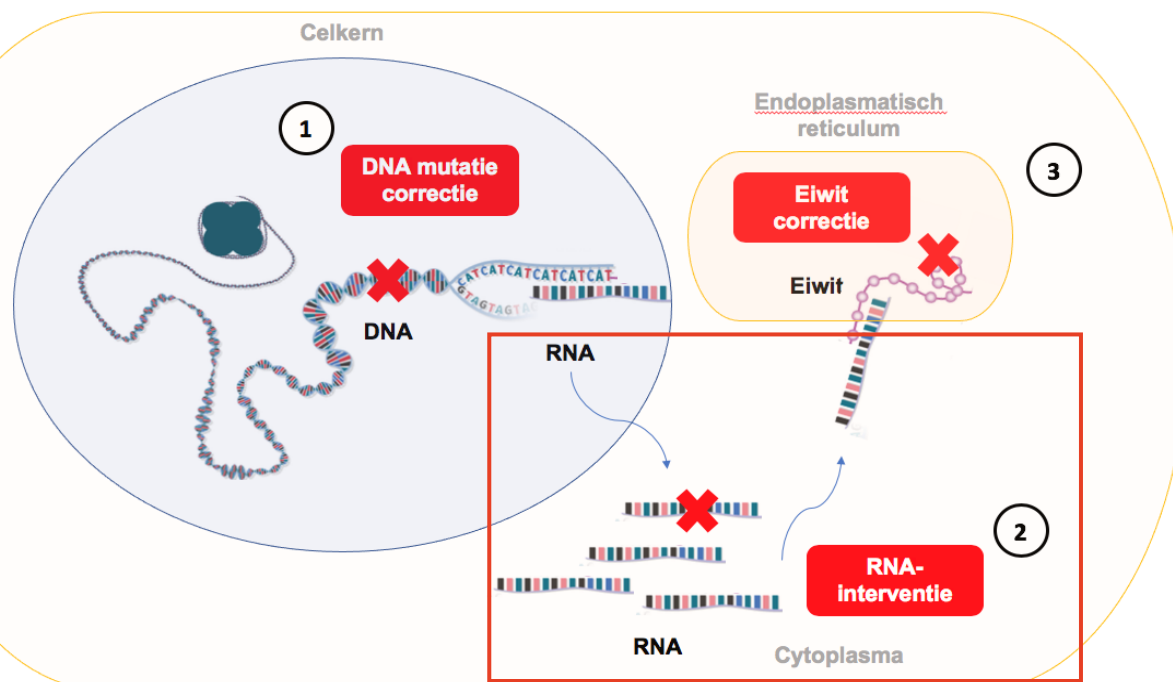


Aptameer

Aptameren - voordelen

	Aptamer	Antibodies
Molecular weight	Small (~12–30 kDa)	Relatively big (~150–180 kDa)
Secondary structures	Various structures: hairpin, loop, G-quadruplex, <i>etc</i>	β -sheets
Generation time	Few hours to months	Several months (~six months)
Batches variations	Low	High
Immunogenicity	Low	High
Minimal target size	Targets small sizes ~60 Da	~600 Da
Targets	Wide range of targets	Immunogenic molecules
Shelf life	Long	Short
Allowed chemical modifications	Various modifications	Limited modifications
Nuclease degradation	Sensitive	Resistant
In vivo half-life	Short (~20 min)	Long (~one month)
Stability	Very stable	Sensitive to temperature and pH changes
Cost	Lower	Higher

RNA 'afvangen'



Adapted from: <https://www.garvan.org.au/research/kinghorn-centre-for-clinical-genomics/learn-about-genomics/dna-base/collection1/dna-chromosomes-and-cells>

Short interfering RNA

Ioannis Karakikes
Stanford

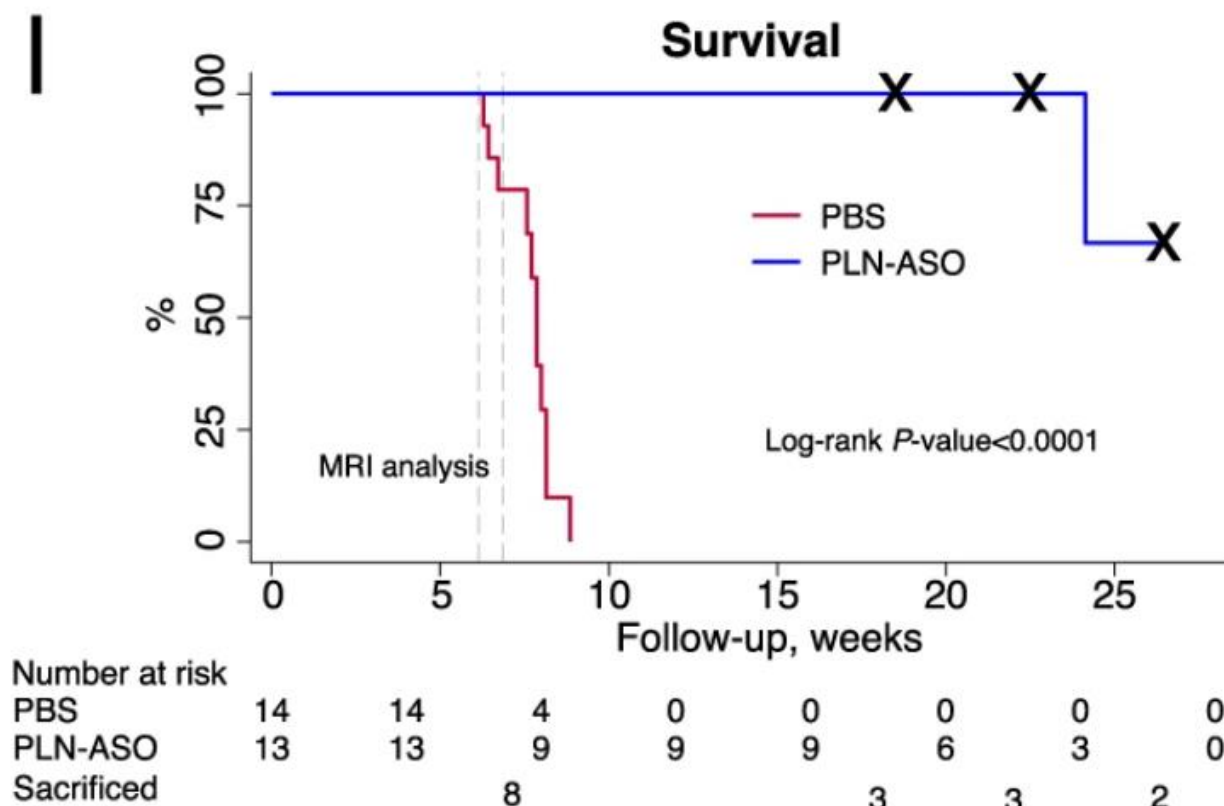
Short hairpin RNA

Anke Tijssen
Yigal Pinto
Amsterdam UMC

Antisense RNA

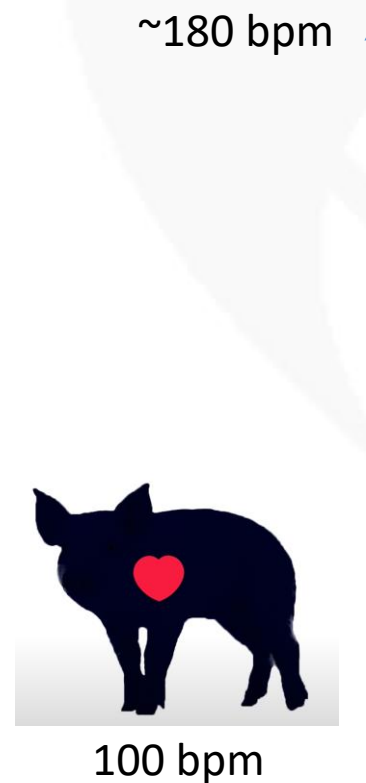
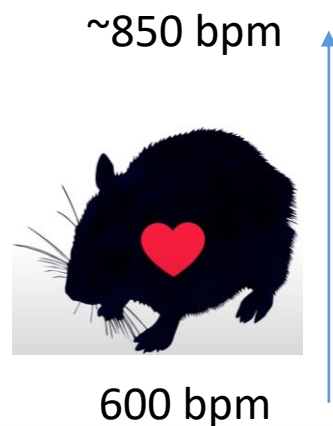
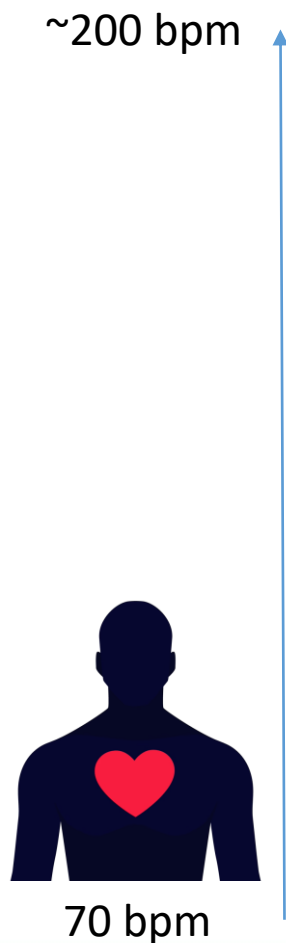
Niels Grote Beverborg
Rudolf de Boer
UMC Groningen

Antisense RNA

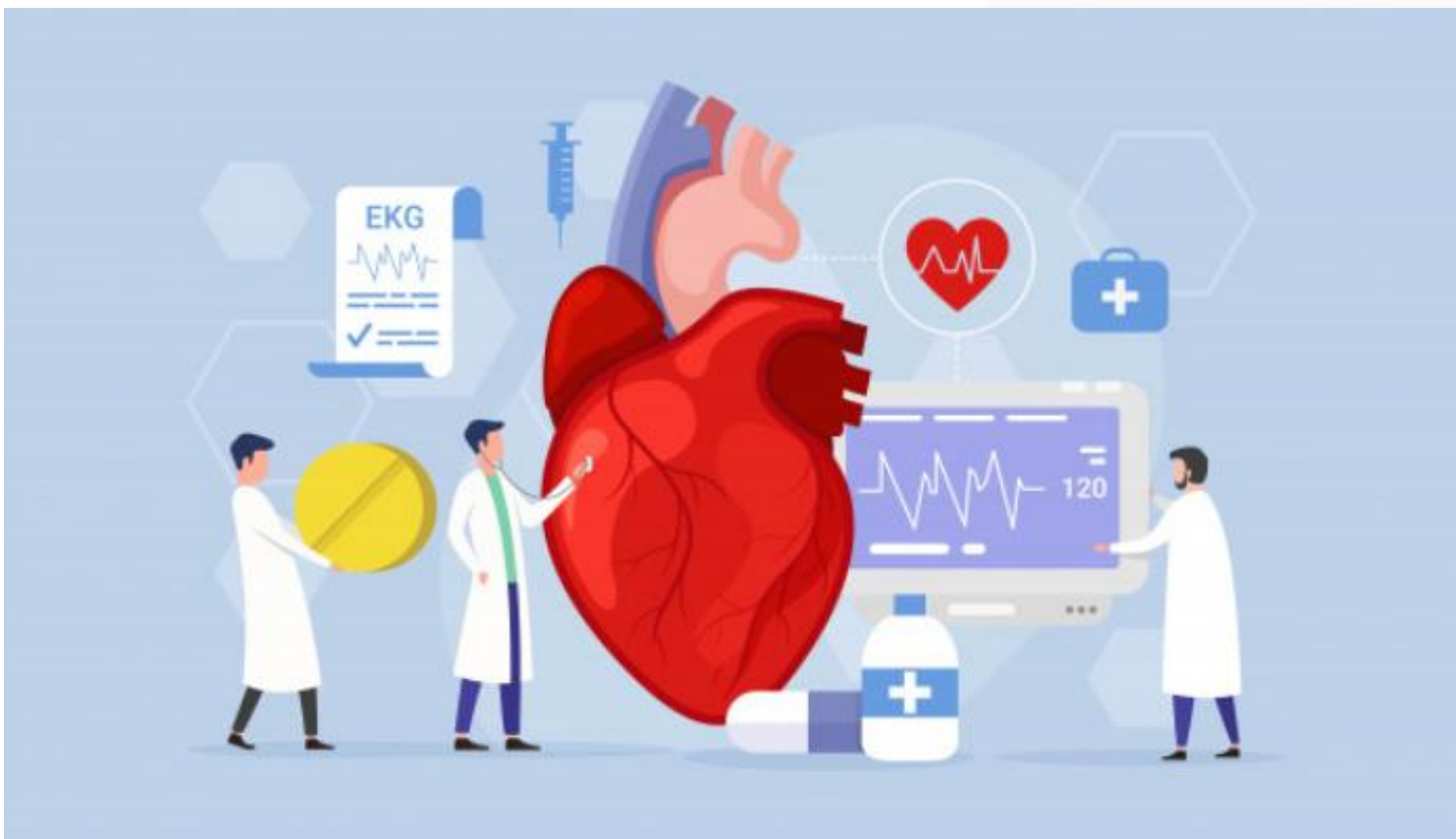


Grote Beverborg, 2021

Muizenhart en mensenhart



Conclusie



Vragen?

