Spædbarnsmord eller hjerterytmeforstyrrelse?

Krimiudgaven af moderne forskningsbaseret personlig medicin

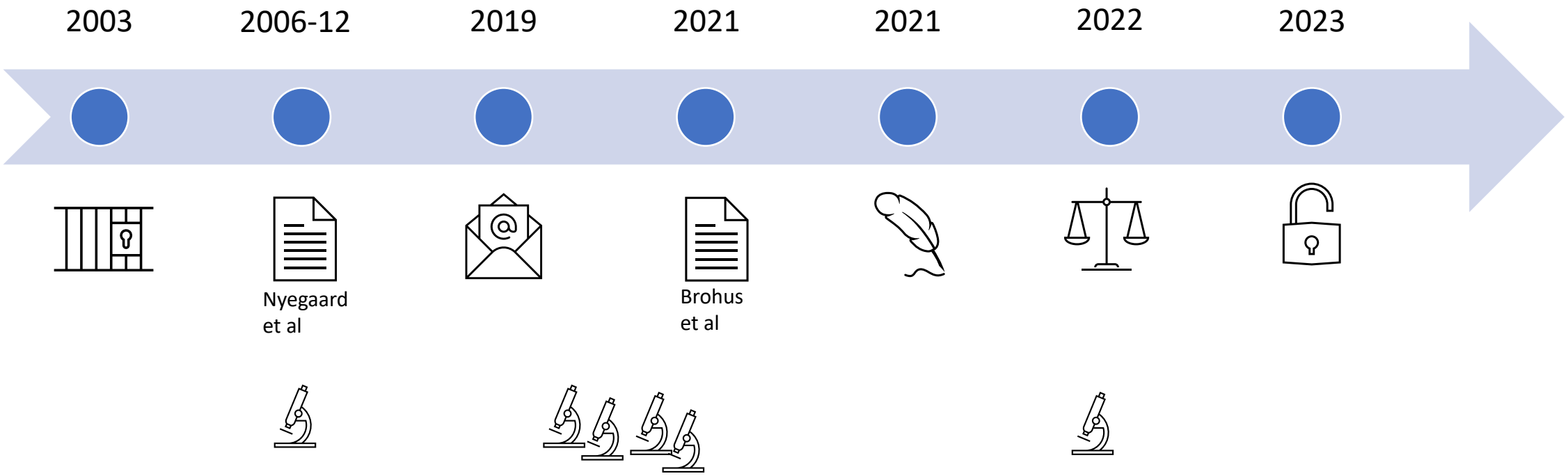
Professor Michael Toft Overgaard, BIO, AAU

Helene H. Jensen

Malene Brohus

Mette Nyegaard

Aftenens menu



Historien bag Kathleen Folbiggs morddom

1987:
Kathleen og
Craig Folbigg
bliver gift

1-2-1989:
Caleb
bliver født

20-2-1989:
Caleb dør
(19 dage)

3-6-1990:
Patrick
bliver født

13-2-1991:
Patrick dør
(8 mdr)

14-10-
1992:
Sarah
bliver født

30-8-1993:
Sarah dør
(10 mdr)

7-8-1997:
Laura
bliver født

1-3-1999:
Laura dør
(18 mdr)

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2001:
Kathleen Folbigg anholdes og anklages for mord

- Kathleen og Craigs forhold opløses.
- Craig finder Kathleens dagbøger og melder hende til politiet.

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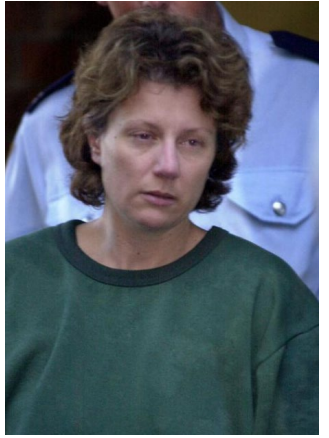
Kathleen Folbigg dømmes skyldig i firedobbelt barnemord



- Kathleen og Craigs forhold opløses.
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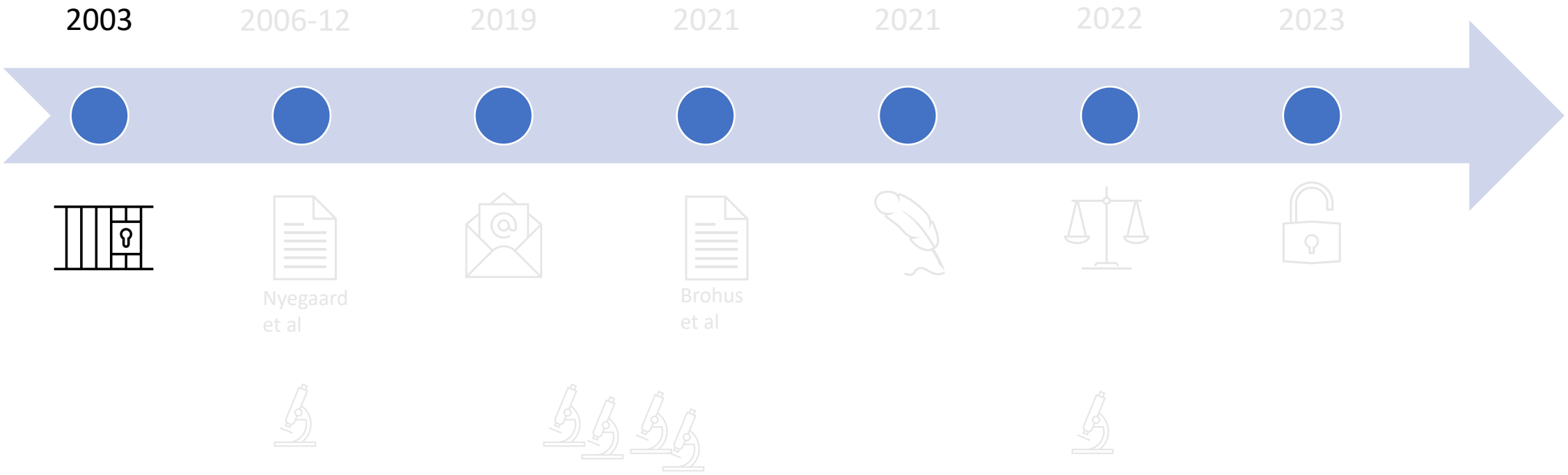
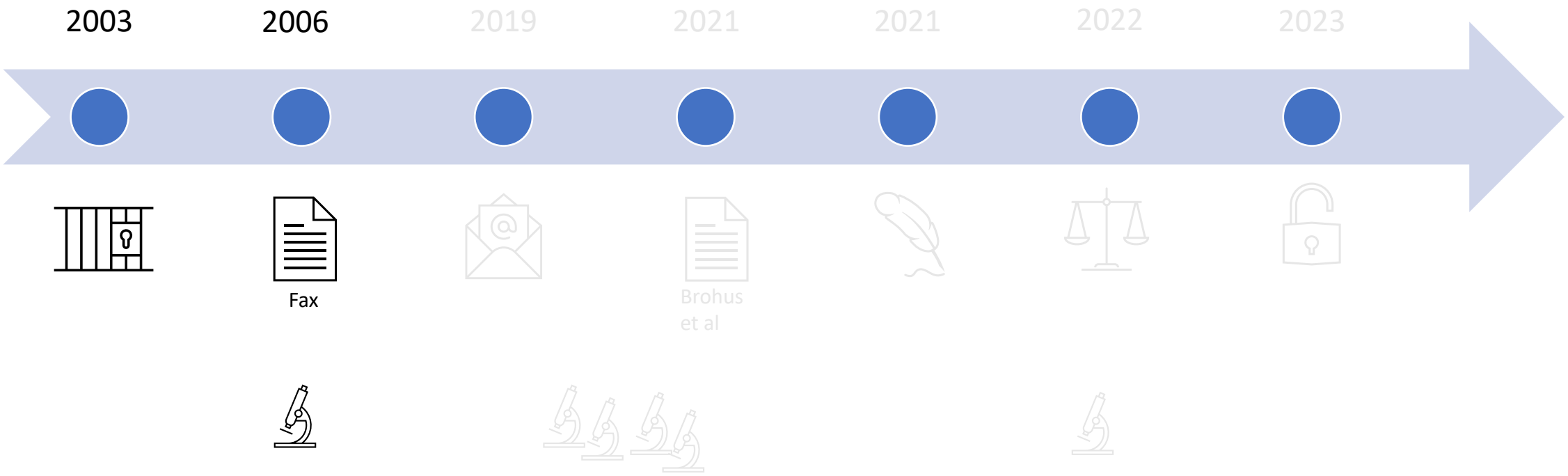
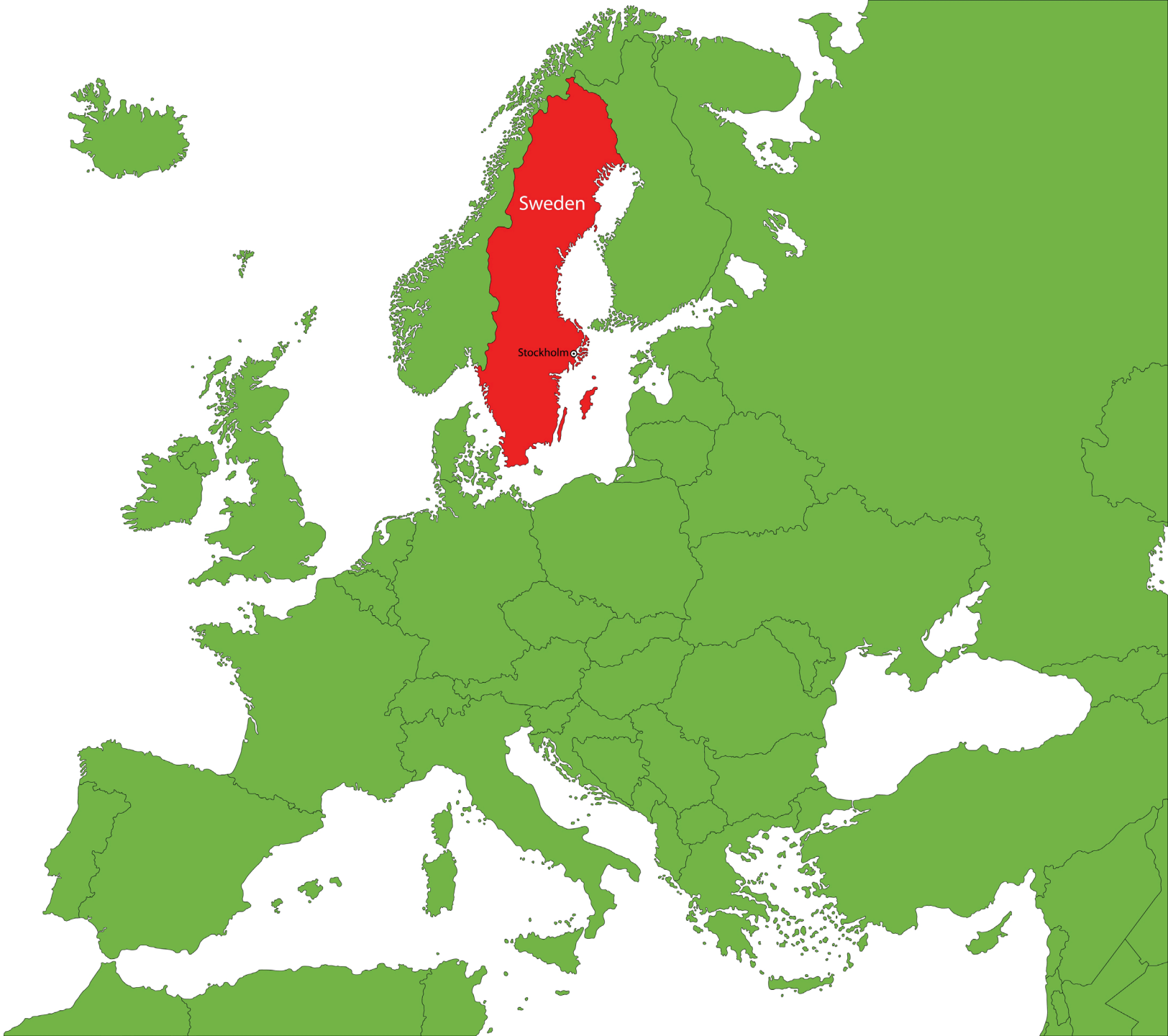
Kathleen idømt 40 års fængsel

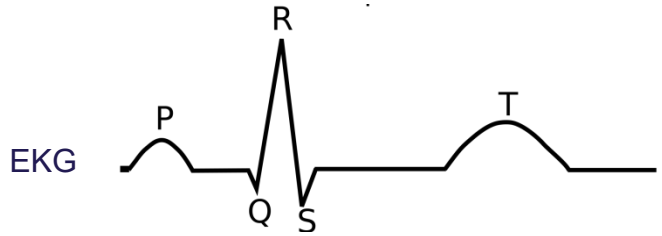


Hvorfor blev vi involveret?



1988

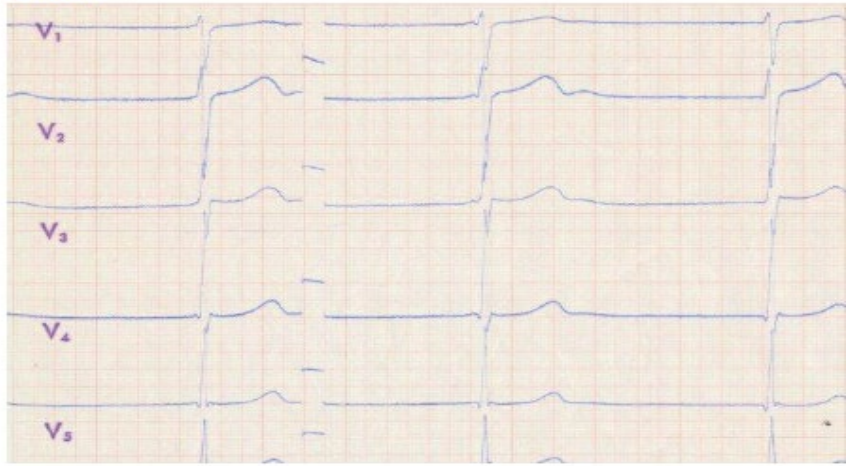




Elektro**K**ardio**G**ram (hjertediagram)

- Dreng med hyppige besvimelser under motion eller stress
- Hjertet ser normalt ud ved scanning
- EKG normalt i hvile (prominent U bølge)
- Hjerterytmeforstyrrelser under sport
- CPVT: Catecholaminergic polymorphic ventricular tachycardia
- Mange tilfælde i familien

EKG i hviletilstand (inaktiv)



EKG under fodboldtræning (12 år gammel)

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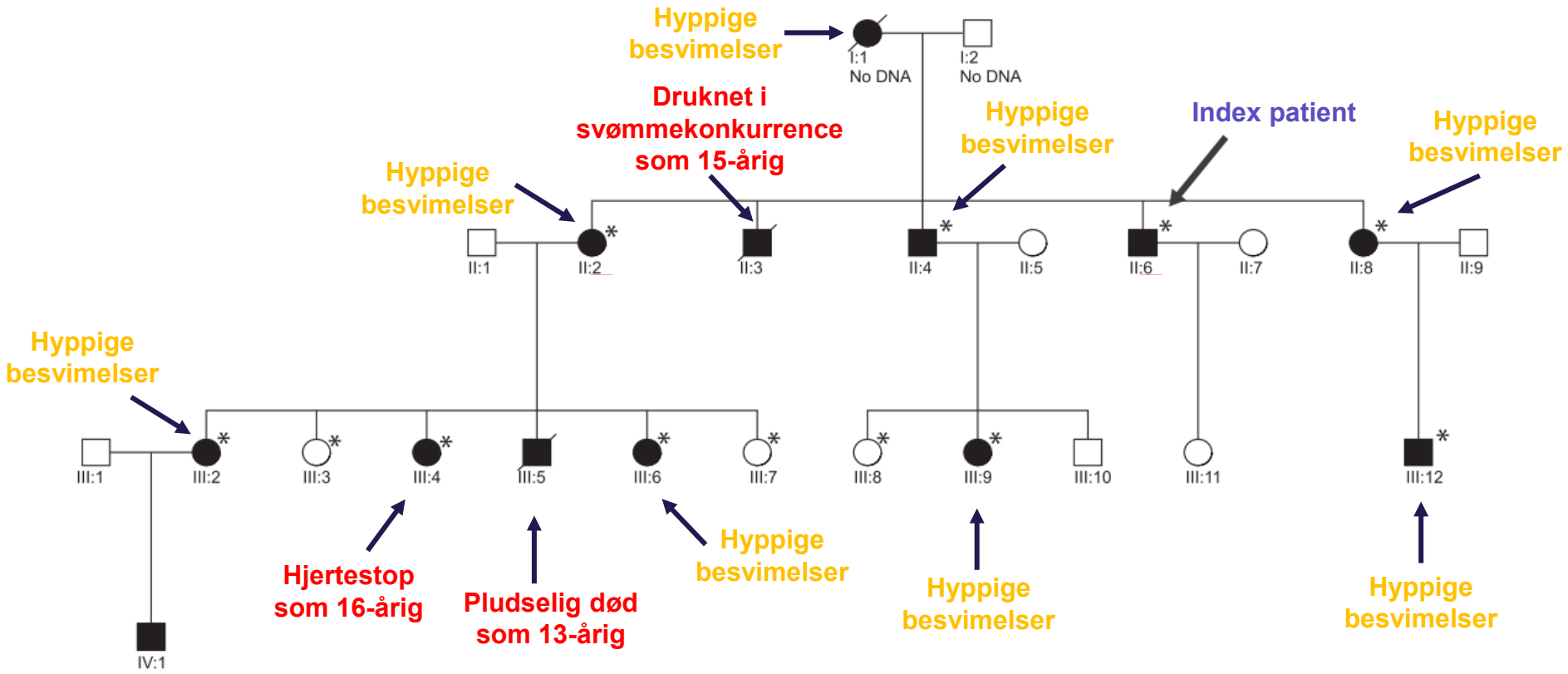
Dominant mendelsk nedarvet sygdom



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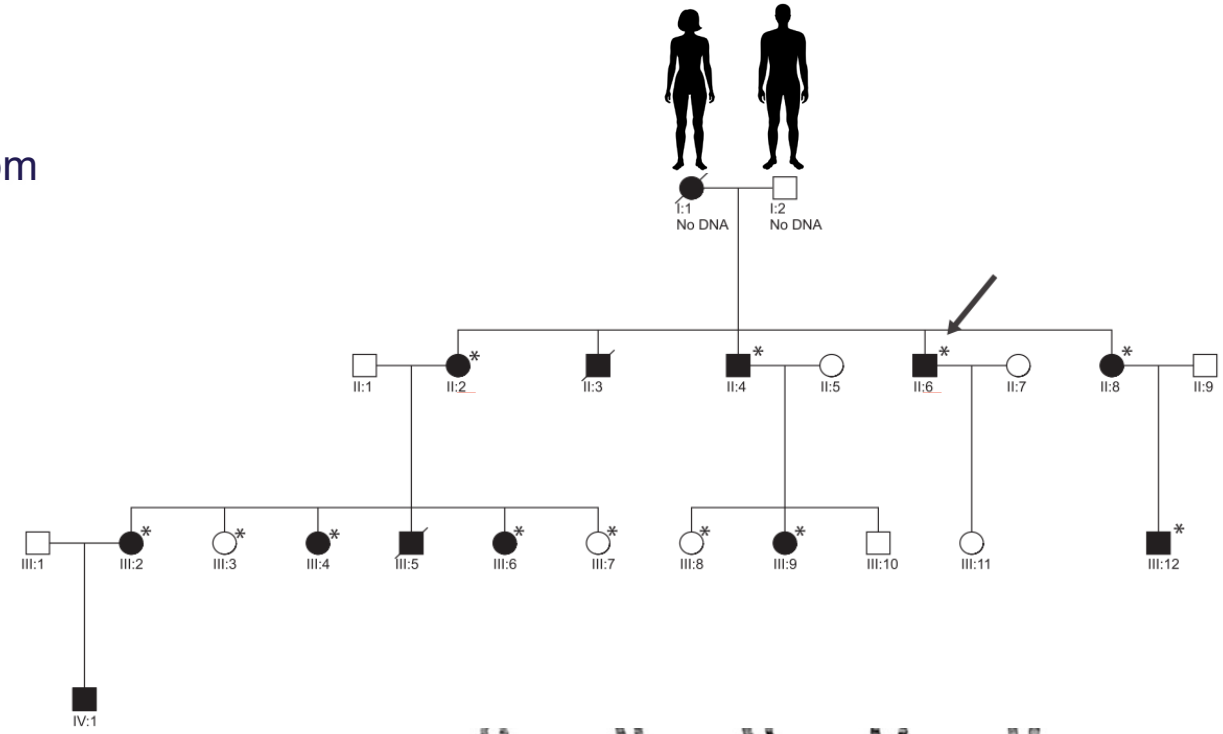
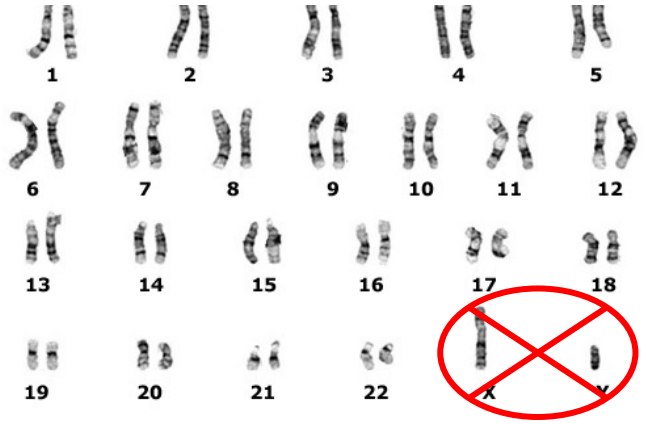
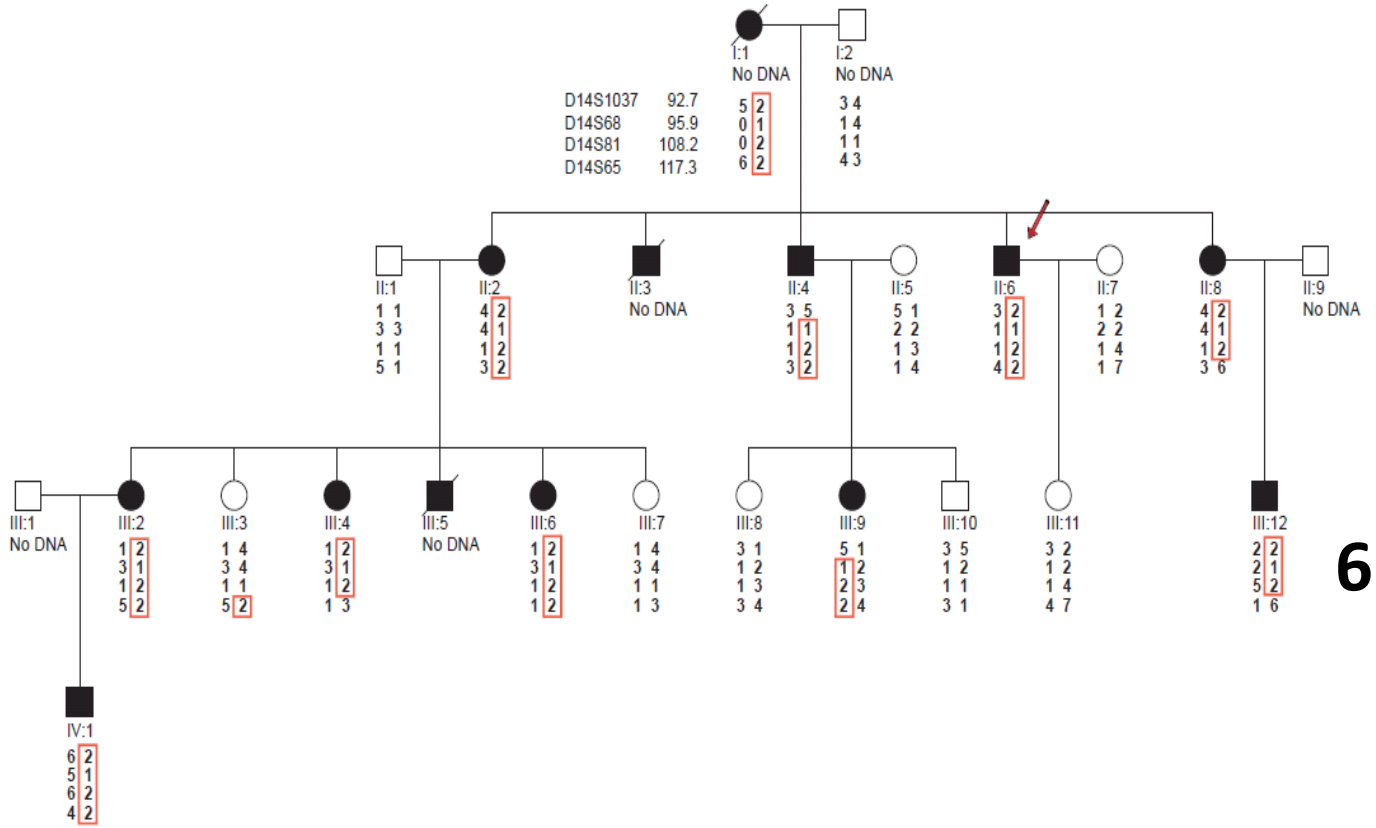
Koblingsanalyse: identificér sygdomsgen

- Stor familie, hvor der optræder en arvelig sygdom
- DNA fra mange familiemedlemmer (*)
- Markørdata (SNPs)
- Screen nedarvning af hvert kromosom
- Identificér område på kromosom, hvor nedarvning stemmer med sygdomsbillede



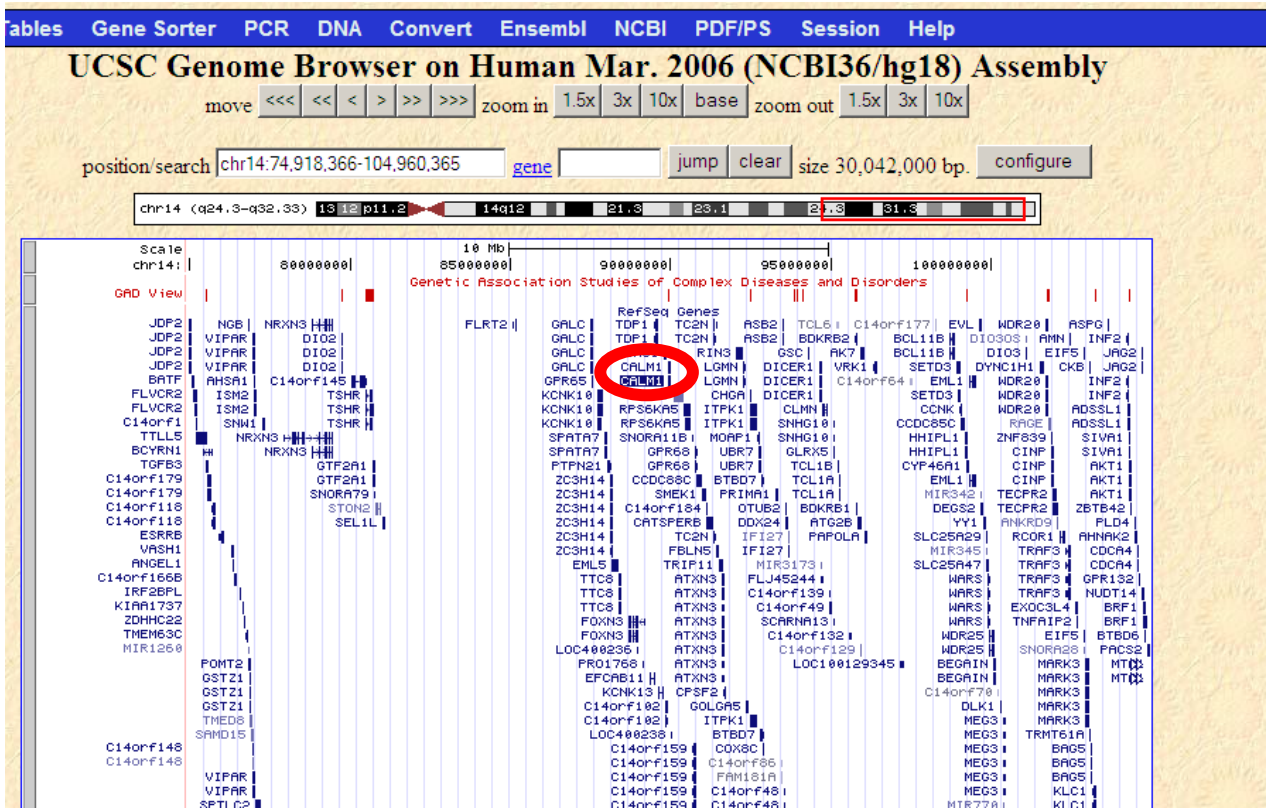


Kromosom 14 nedarves med sygdommen



65 gener!

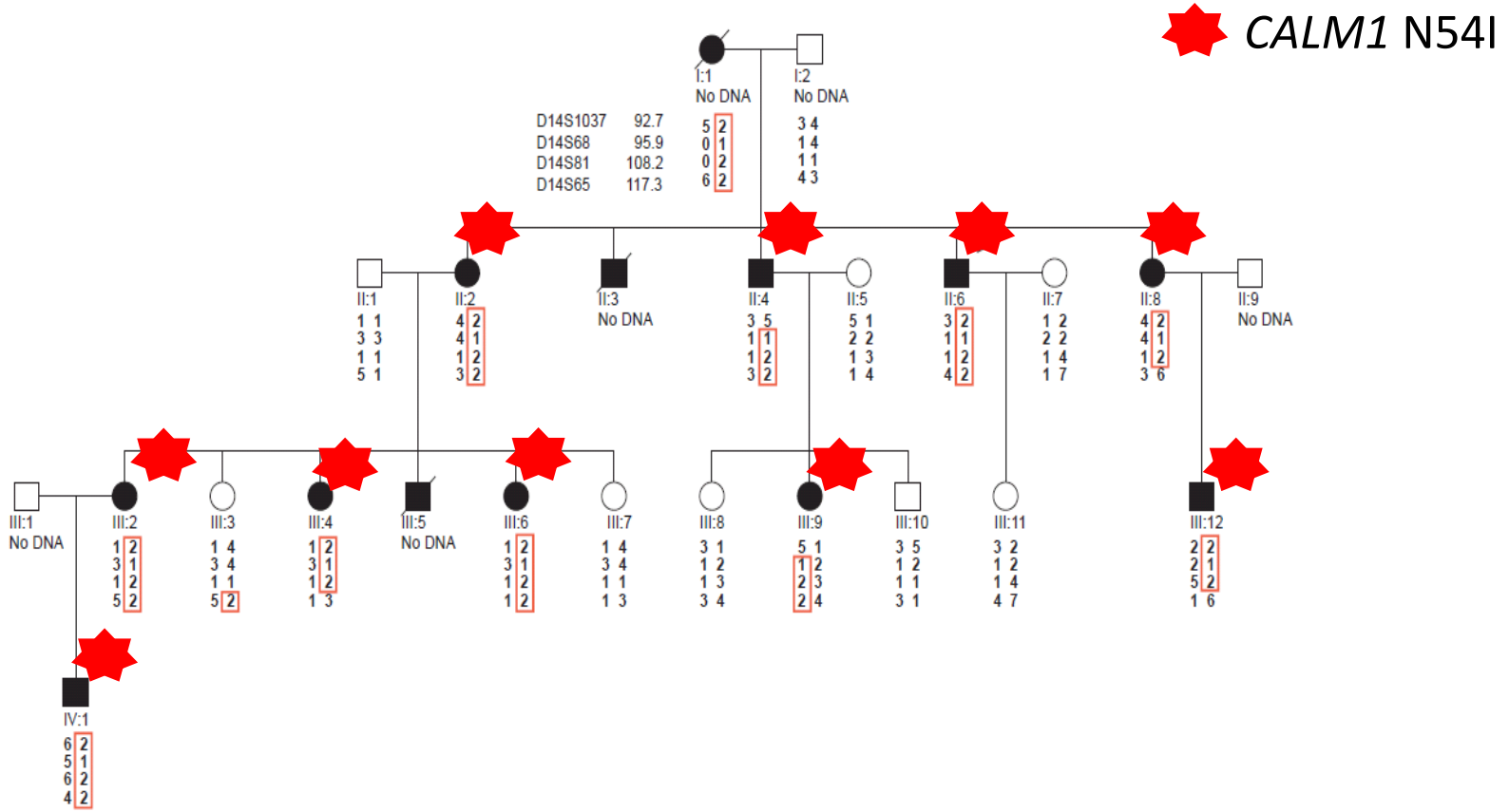
Jagten på det rigtige gen (blandt 65 kandidater)



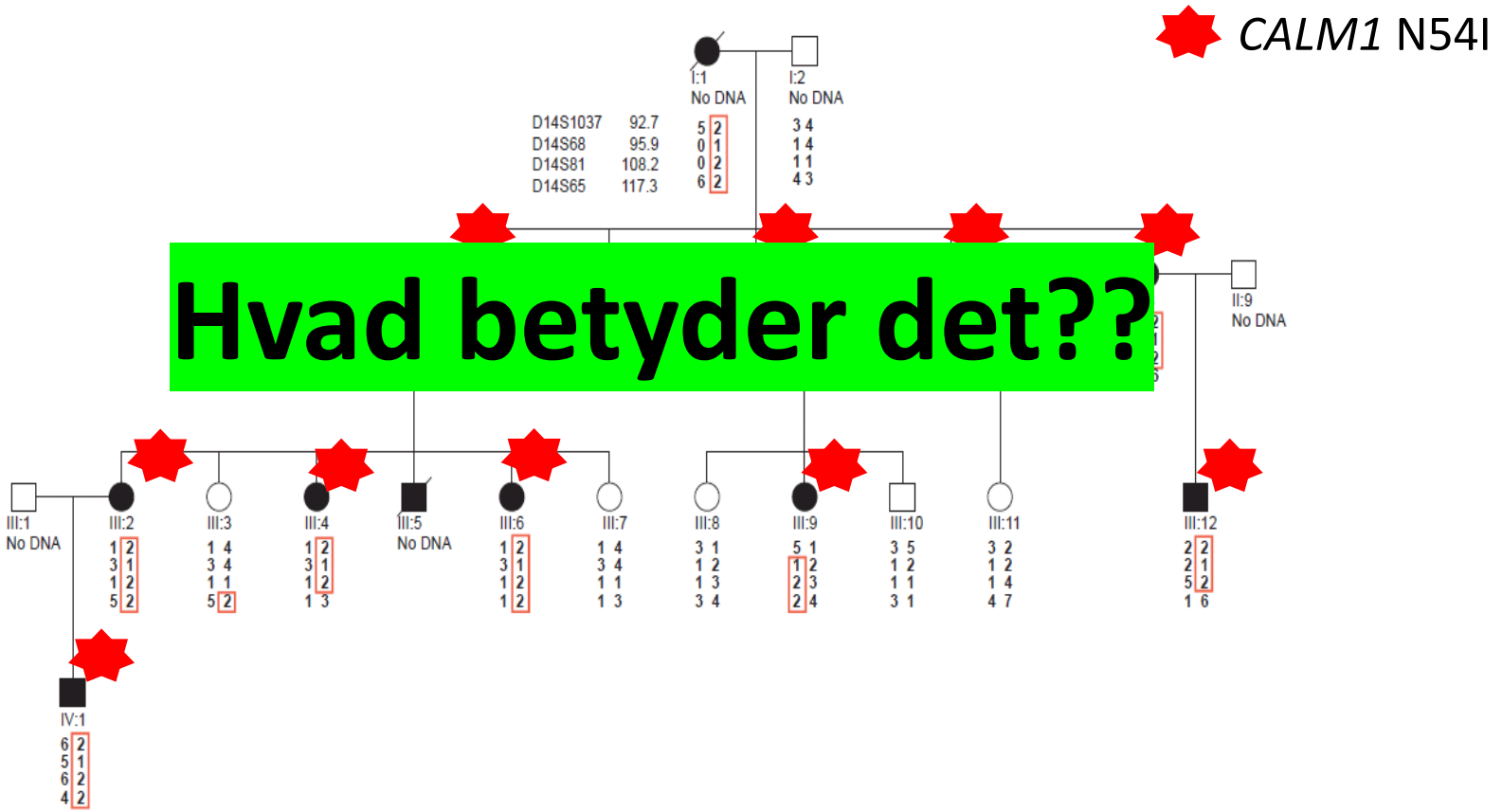
Sekventér de 6 exons i *CALM1* genet

A small gene, going almost unnoticed, because there is no interesting variation in it

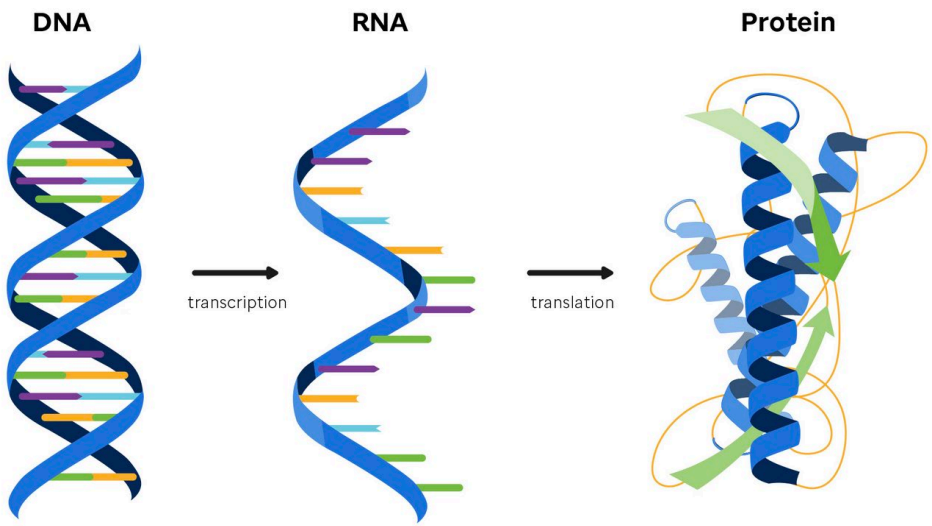
Første mutation nogensinde observeret i *CALM1*



Første mutation nogensinde observeret i *CALM1*



Det centrale dogme i molekylærbiologi



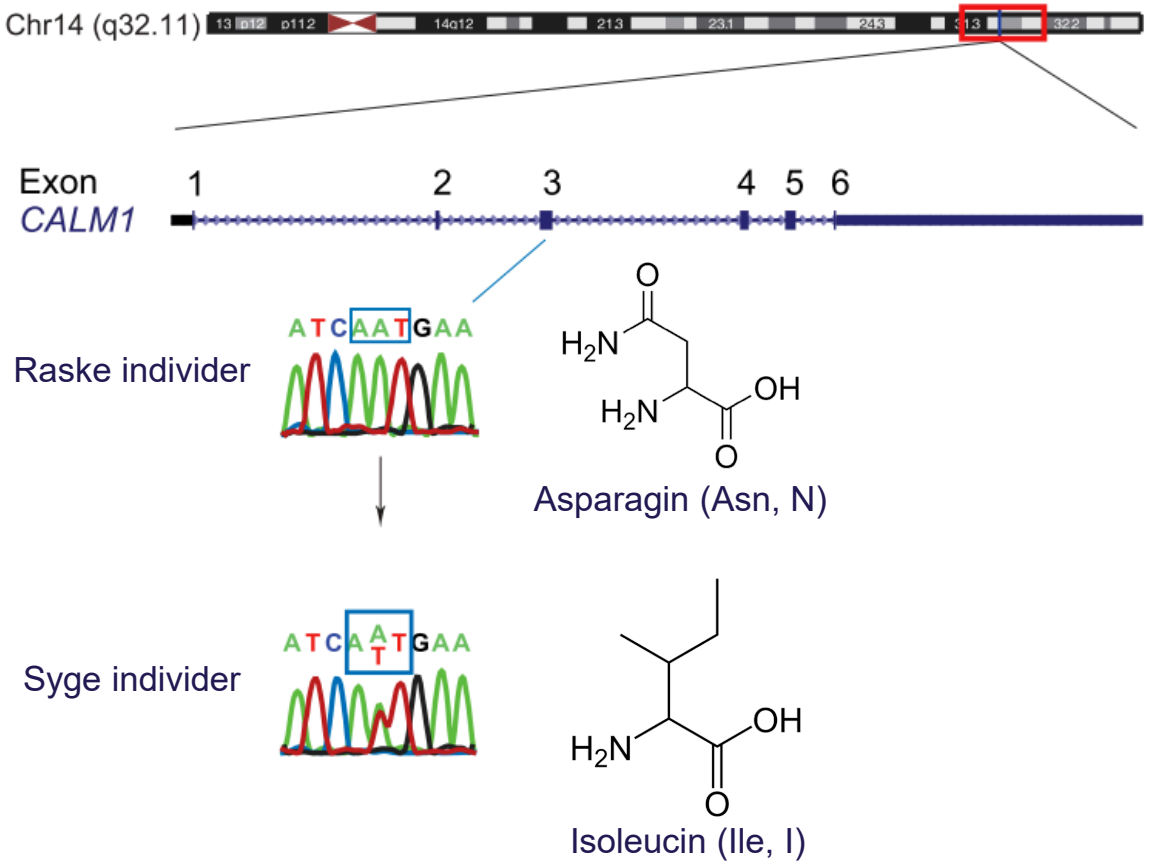
Genetisk variant (missense)

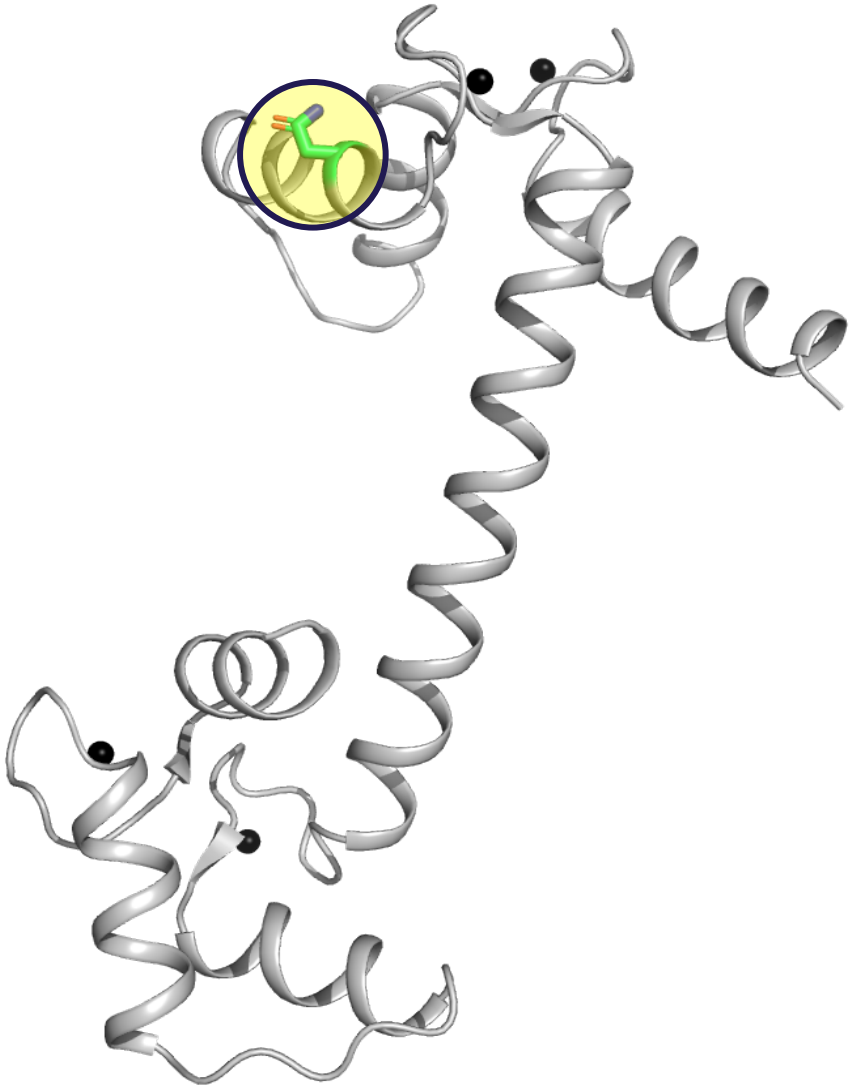
Effect på protein

Variant på DNA niveau (ændring i basepar)

Variant på protein niveau (ændring i aminosyrer)

Den første *CALM1* mutation nogensinde (ændring i opskriften for calmodulin proteinet)





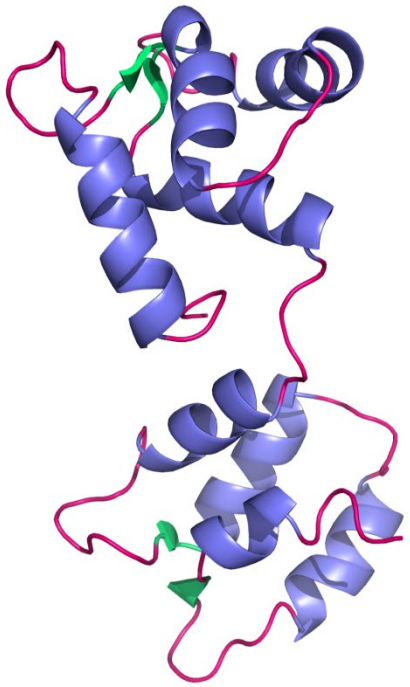
Jagten på *CALM1* mutation nr 2

Kassen med uforklarede hjerte arytmier
Prof Michael Christiansen, SSI

CALM1 N98S
de novo
CPVT-lignende

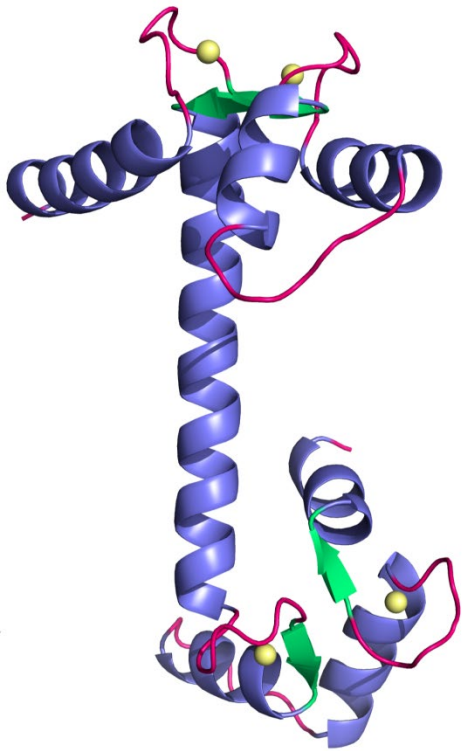
Calmodulin: et alsidigt calcium-bindende protein

Ca^{2+}-frit



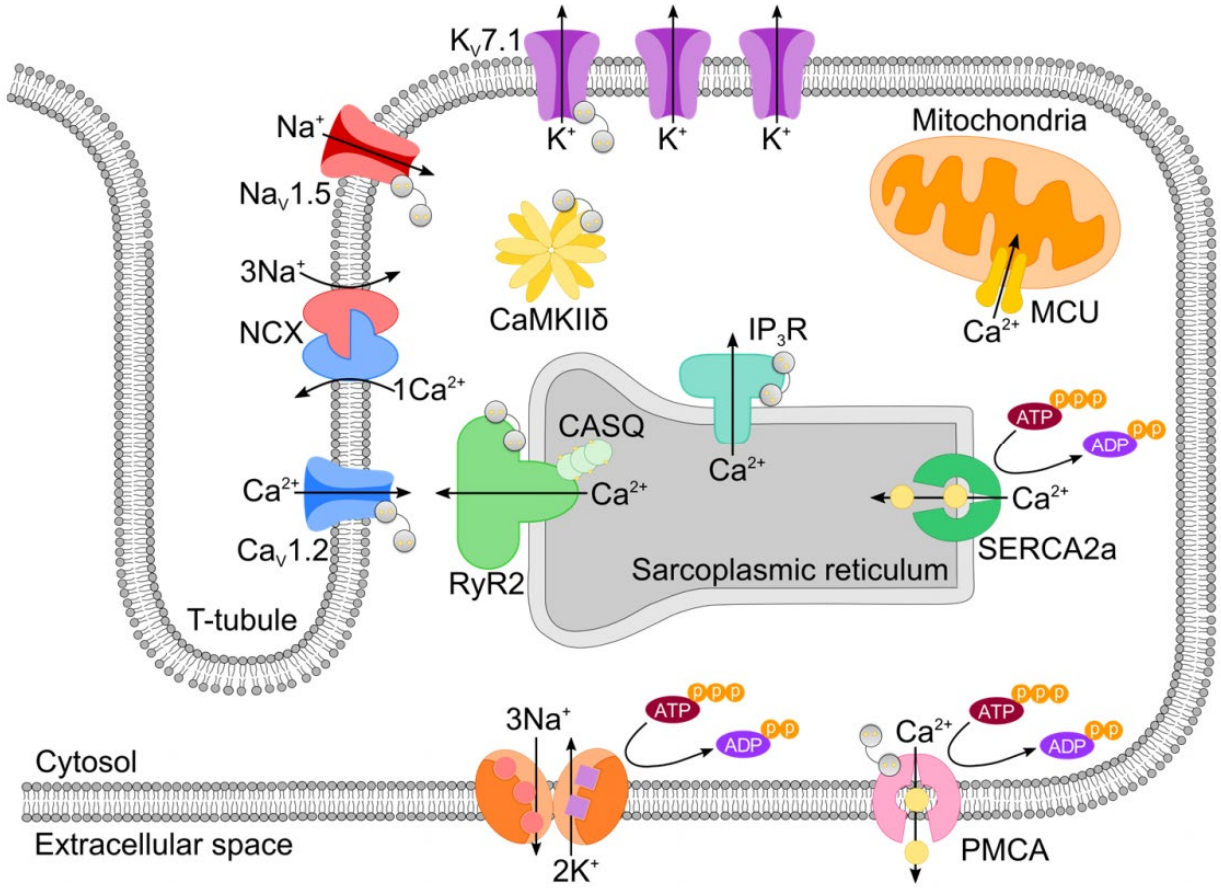
Apo-CaM

Ca^{2+}-bundet



Ca^{2+}-CaM

Vekselvirkninger i en celle



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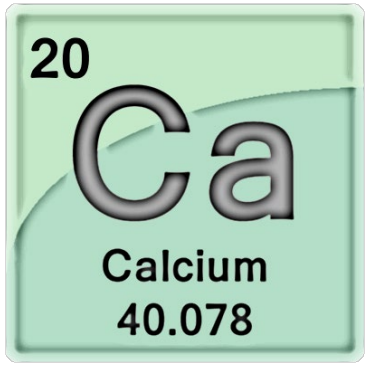
Calcium: et cellulært signal

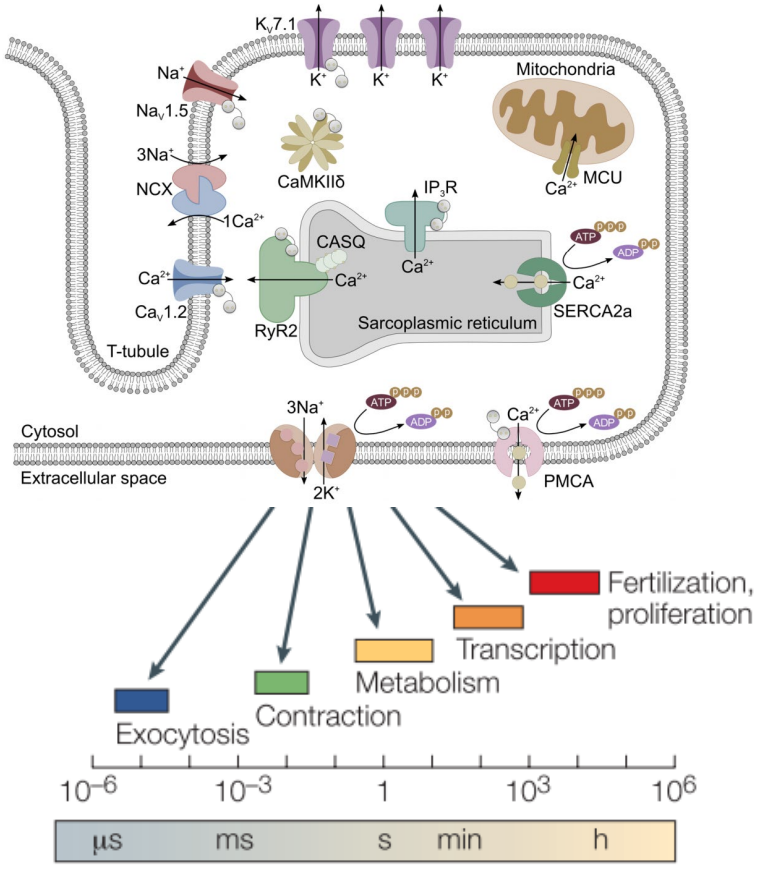
Ca^{2+}-signal



Ca^{2+}-signal oversætter

?

Ca^{2+}-signal respons



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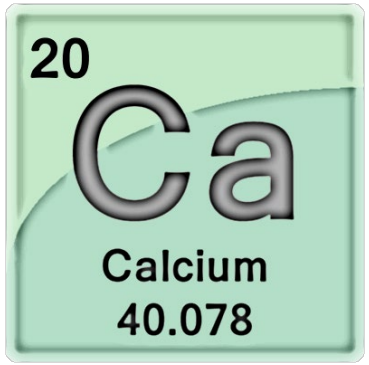
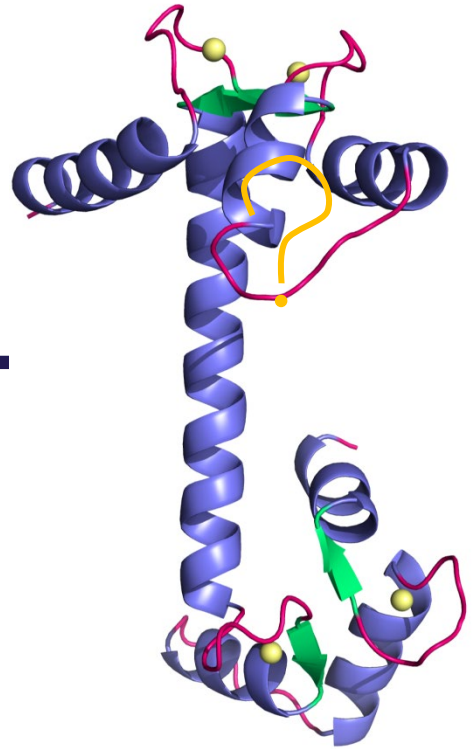
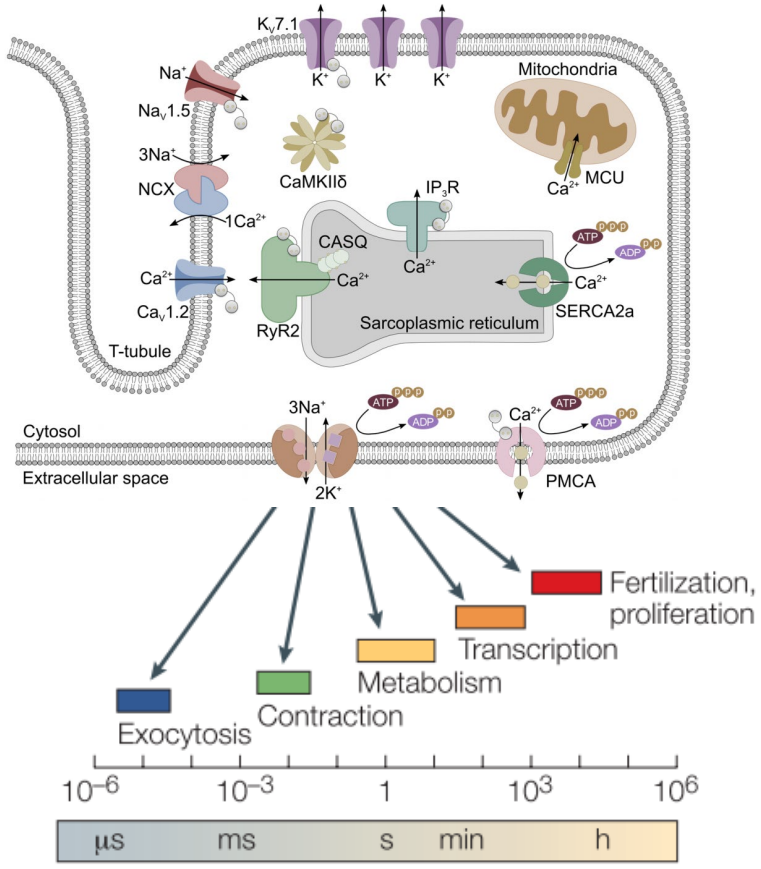


Ca^{2+}-signal oversætter

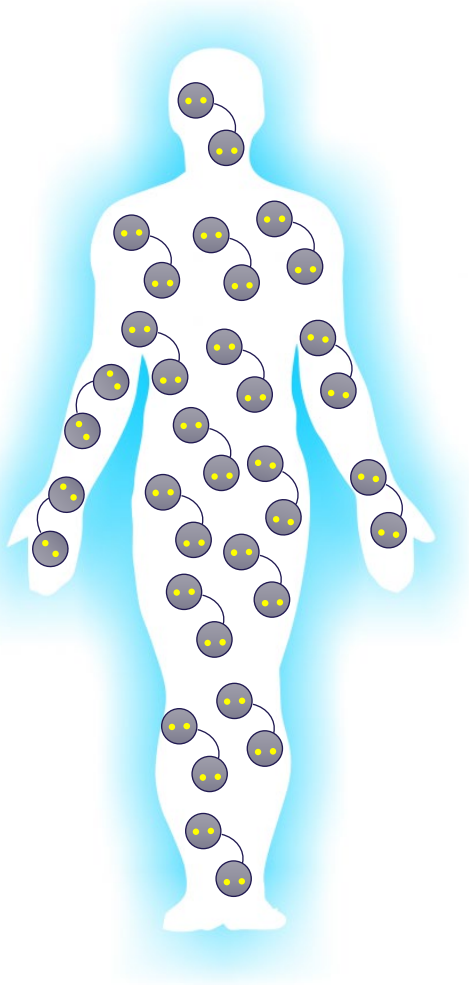


Ca^{2+}-signal respons



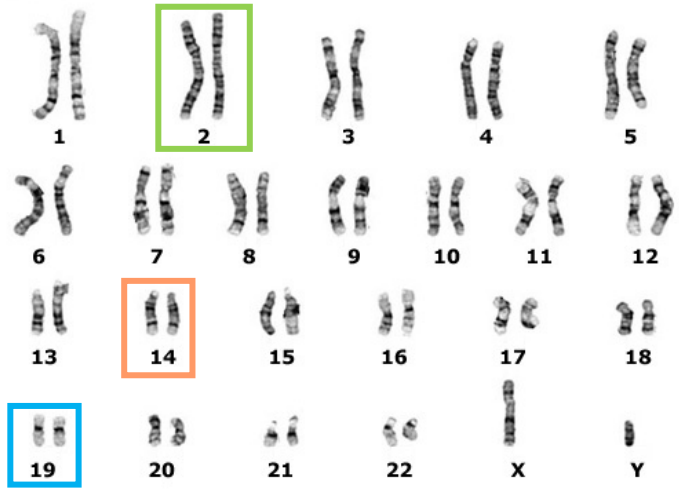
Calmodulin er unik

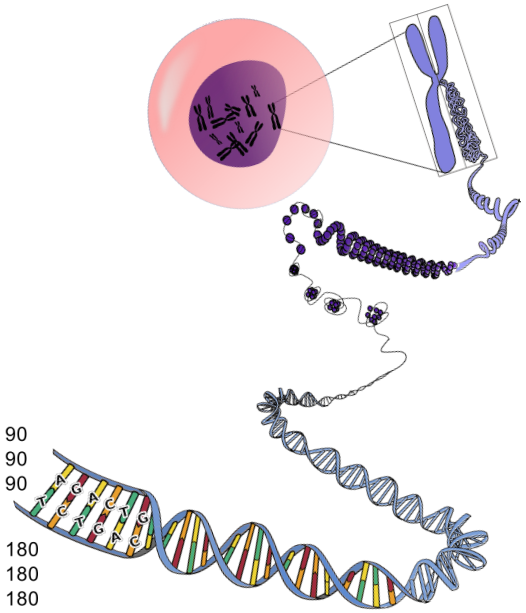
- Findes overalt i kroppen.



Calmodulin er unik

- Findes overalt i kroppen.
- Mennesker har tre gener (*CALM1-3*).





```
CALM1 (kromosom 14)  ATGGCTGATC AGCTGACCGA AGAACAGATT GCTGAATTCA AGGAAGCCTT CTCCCTATTT GATAAAGATG GCGATGGCAC CATCACAACA 90
CALM2 (kromosom 2)   ATGGCTGACC AACTGACTGA AGAGCAGATT GCAGAATTCA AAGAAGCTTT TTCACTATTT GACAAAGATG GTGATGGAAC TATAACAACA 90
CALM3 (kromosom 19)  ATGGCTGACC AGCTGACTGA GGAGCAGATT GCAGAGTTCA AGGAGGCCTT CTCCCTCTTT GACAAGGATG GAGATGGCAC TATCACCACC 90
                                100                             120                             140                             160                             180
CALM1 (kromosom 14)  AAGGAACTTG GAACTGTCAT GAGGTCACTG GGTCAGAACC CAACAGAAGC TGAATTGCAG GATATGATCA ATGAAGTGGA TGCTGATGGT 180
CALM2 (kromosom 2)   AAGGAATTGG GAACTGTAAT GAGATCTCTT GGGCAGAATC CCACAGAAGC AGAGTTACAG GACATGATTA ATGAAGTAGA TGCTGATGGT 180
CALM3 (kromosom 19)  AAGGAGTTGG GGACAGTGAT GAGATCCCTG GGACAGAACC CCACTGAAGC AGAGCTGCAG GATATGATCA ATGAGGTGGA TGCAGATGGG 180
                                200                             220                             240                             260
CALM1 (kromosom 14)  AATGGCACCA TTGACTTCCC CGAATTTTTG ACTATGATGG CTAGAAAAAT GAAAGATACA GATAGTGAAG AAGAAATCCG TGAGGCATTC 270
CALM2 (kromosom 2)   AATGGCACAA TTGACTTCCC TGAATTTCTG ACAATGATGG CAAGAAAAAT GAAAGACACA GACAGTGAAG AAGAAATTAG AGAAGCATTC 270
CALM3 (kromosom 19)  AACGGGACCA TTGACTTCCC GGAGTTCCTG ACCATGATGG CCAGAAAGAT GAAGGACACA GACAGTGAGG AGGAGATCCG AGAGGCGTTC 270
                                280                             300                             320                             340                             360
CALM1 (kromosom 14)  CGAGTCTTTG ACAAGGATGG CAATGGTTAT ATCAGTGCAG CAGAACTACG TCACGTCATG ACAAACTTAG GAGAAAACT AACAGATGAA 360
CALM2 (kromosom 2)   CGTGTGTTTG ATAAGGATGG CAATGGCTAT ATTAGTGCTG CAGAACTTCG CCATGTGATG ACAAACCTTG GAGAGAAGTT AACAGATGAA 360
CALM3 (kromosom 19)  CGTGTCTTTG ACAAGGATGG GAATGGCTAC ATCAGCGCCG CAGAGCTGCG TCACGTAATG ACGAACCTGG GGGAGAAGCT GACCGATGAG 360
                                380                             400                             420                             440
CALM1 (kromosom 14)  GAAGTAGATG AAATGATCAG AGAAGCAGAT ATTGATGGAG ACGGACAAGT CAACTATGAA GAATTCGTAC AGATGATGAC TGCAAAATGA 450
CALM2 (kromosom 2)   GAAGTTGATG AAATGATCAG GGAAGCAGAT ATTGATGGTG ATGGTCAAGT AAACTATGAA GAGTTTGTAC AAATGATGAC AGCAAAGTGA 450
CALM3 (kromosom 19)  GAGGTGGATG AGATGATCAG GGAGGCTGAC ATCGATGGAG ATGGCCAGGT CAATTATGAA GAGTTTGTAC AGATGATGAC TGCAAAGTGA 450
```

Calmodulin er unik

- Findes overalt i kroppen.

```
                                    20                  40
Menneske  MADQLTEEQI AEFKEAFSLF DKDGDGTITT KELGTVMRSL GQNPTEAELQ 50

                          60                  80                  100
Menneske  DMINEVDADG NGTIDFPEFL TMMARKMKDT DSEEEIREAF RVFDKDGNGY 100

                                   120                 140
Menneske  ISAAELRHVM TNLGEKLTDE EVDEMIREAD IDGDGQVNYE EFVQMMTAK 149
```

- Mennesker har tre gener (*CALM1-3*).
- *CALM1-3* koder for samme protein.

Calmodulin er unik

- Findes overalt i kroppen.

```
                                  20                                  40
                                  |                                   |
Menneske  MADQLTEEQI AEFKEAFSLF DKDGDGTITT KELGTVMRSL GQNPTEAELQ 50
Gris      MADQLTEEQI AEFKEAFSLF DKDGDGTITT KELGTVMRSL GQNPTEAELQ 50
Mus       MADQLTEEQI AEFKEAFSLF DKDGDGTITT KELGTVMRSL GQNPTEAELQ 50
```

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```
                        60                                  80                                 100
                        |                                   |                                  |
Menneske  DMINEVDADG NGTIDFPEFL TMMARKMKDT DSEEEIREAF RVFDKDGNGY 100
Gris      DMINEVDADG NGTIDFPEFL TMMARKMKDT DSEEEIREAF RVFDKDGNGY 100
Mus       DMINEVDADG NGTIDFPEFL TMMARKMKDT DSEEEIREAF RVFDKDGNGY 100
```

- Proteinet er evolutionært bevaret.

```
                                 120                                 140
                                  |                                   |
Menneske  ISAAELRHVM TNLGEKLTDE EVDEMIREAD IDGDGQVNYE EFVQMMTAK 149
Gris      ISAAELRHVM TNLGEKLTDE EVDEMIREAD IDGDGQVNYE EFVQMMTAK 149
Mus       ISAAELRHVM TNLGEKLTDE EVDEMIREAD IDGDGQVNYE EFVQMMTAK 149
```

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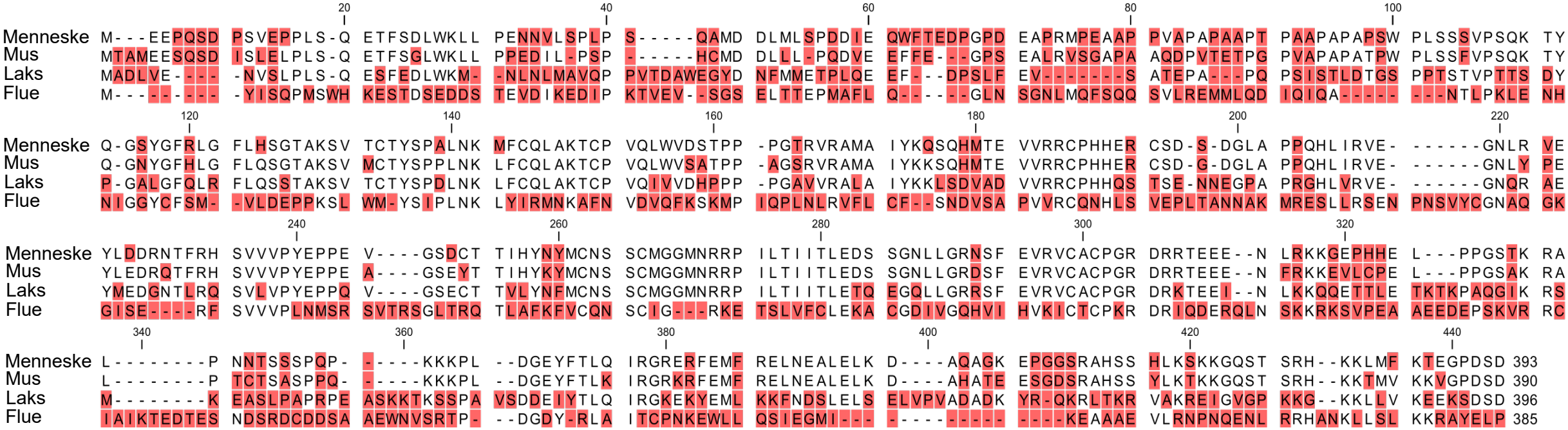
```
                                                  20                                                  40
                                                  |                                                   |
Menneske  MADQLTEEQI AEFKEAFSLF DKDGDGTITT KELGTVMRSL GQNPTEAELQ 50
Gris      MADQLTEEQI AEFKEAFSLF DKDGDGTITT KELGTVMRSL GQNPTEAELQ 50
Mus       MADQLTEEQI AEFKEAFSLF DKDGDGTITT KELGTVMRSL GQNPTEAELQ 50
Laks      MADQLTEEQI AEFKEAFSLF DKDGDGTITT KELGTVMRSL GQNPTEAELQ 50
Flue      MADQLTEEQI AEFKEAFSLF DKDGDGTITT KELGTVMRSL GQNPTEAELQ 50
Kornblomst MADQLTDEQI SEFKEAFSLF DKDGDGCITT KELGTVMRSL GQNPTEAELQ 50
Gær       MSSNLTEEQI AEFKEAFALF DKDNNGSISS SELATVMRSL GLSPSEAEVN 50
                                  60                  80                                  100
                                  |                   |                                   |
Menneske  DMINEVDADG NGTIDFPEFL TMMARKMKDT DSEEEIREAF RVFDKDGNGY 100
Gris      DMINEVDADG NGTIDFPEFL TMMARKMKDT DSEEEIREAF RVFDKDGNGY 100
Mus       DMINEVDADG NGTIDFPEFL TMMARKMKDT DSEEEIREAF RVFDKDGNGY 100
Laks      DMINEVDADG NGTIDFPEFL TMMARKMKDT DSEEEIREAF RVFDKDGNGY 100
Flue      DMINEVDADG NGTIDFPEFL TMMARKMKDT DSEEEIREAF RVFDKDGNGF 100
Kornblomst DMINEVDADG NGTIDFPEFL NLMAKKMKDT DSEEELKEAF RVFDKDQNGF 100
Gær       DLMNEIDVDG NHQIEFSEFL ALMSRQLKSN DSEQELLEAF KVFDKNGDGL 100
                                                 120                                                 140
                                                  |                                                   |
Menneske  ISAAELRHVM TNLGEKLTDE EVDEMIREAD IDGDGQVNYE EFVQMMTAK 149
Gris      ISAAELRHVM TNLGEKLTDE EVDEMIREAD IDGDGQVNYE EFVQMMTAK 149
Mus       ISAAELRHVM TNLGEKLTDE EVDEMIREAD IDGDGQVNYE EFVQMMTAK 149
Laks      ISAAELRHVM TNLGEKLTDE EVDEMIREAD IDGDGQVNYE EFVQMMTAK 149
Flue      ISAAELRHVM TNLGEKLTDE EVDEMIREAD IDGDGQVNYE EFVTMMTSK 149
Kornblomst ISAAELRHVM TNLGEKLTDE EVEEMIREAD VDGDGQINYE EFVKIMMAK 149
Gær       ISAAELKHVL TSIGEKLTDA EVDDMLREVS -DGSGEINIQ QFAALL-SK 147
```

Calmodulin er unik – p53 til sammenligning



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Almen overbevisning:

calmodulin tolererer ingen variation!


1. NG preliminary
2. NEJM
3. Lancet
4. Nature Genetics
5. JCI
6. Circulation
7. AJHG
Publish

“If it is as conserved as the authors claim,

CALM variants must be incompatible with life”

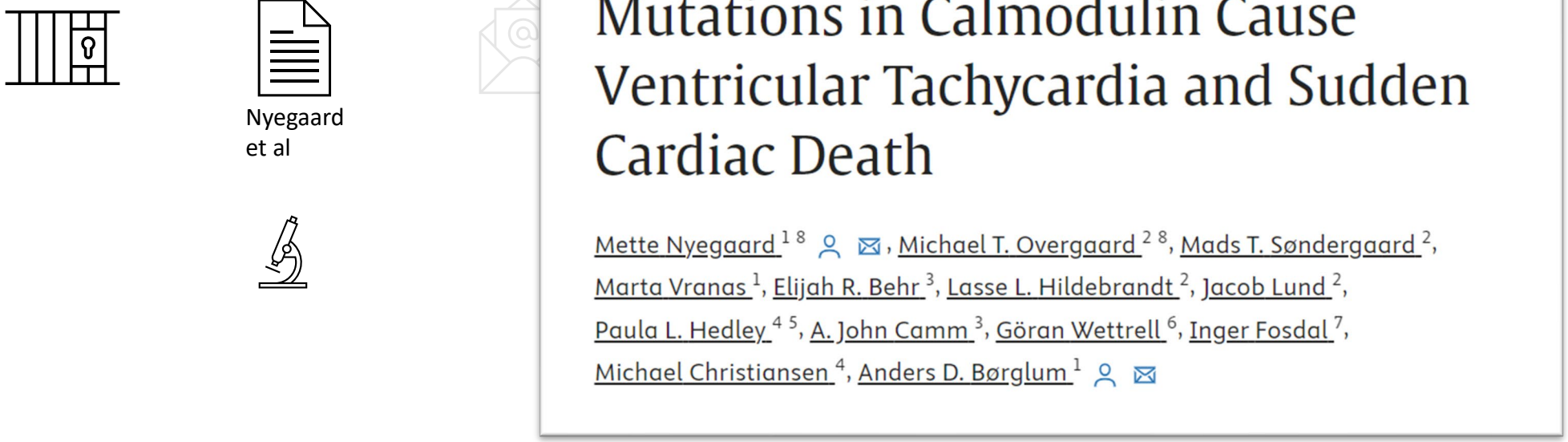
Reviewer

Mutationer i Calmodulin gener giver pludselig hjertedød

2003

2006-12

Nyegaard et al



AJHG

CellPress

Volume 91, Issue 4, 5 October 2012, Pages 703-712

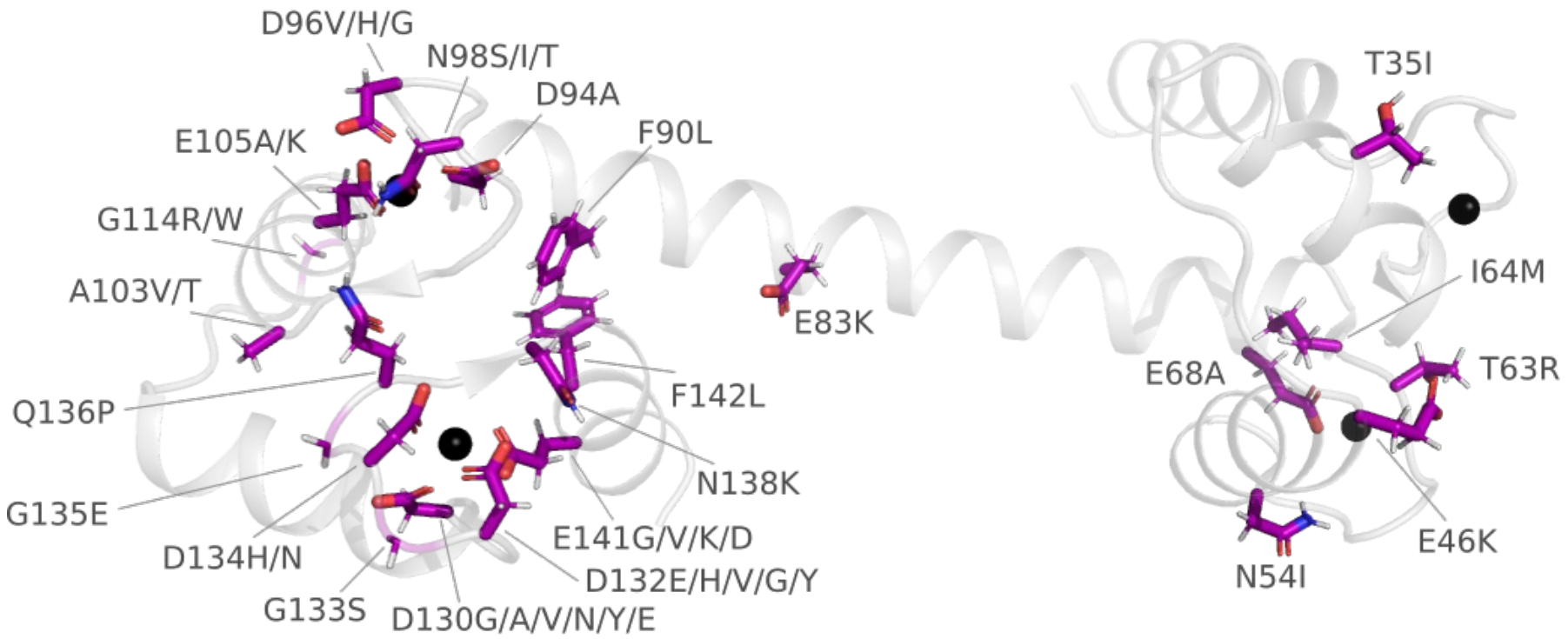
Report

Mutations in Calmodulin Cause Ventricular Tachycardia and Sudden Cardiac Death

Mette Nyegaard [1 8], Michael T. Overgaard [2 8], Mads T. Søndergaard [2], Marta Vranas [1], Elijah R. Behr [3], Lasse L. Hildebrandt [2], Jacob Lund [2], Paula L. Hedley [4 5], A. John Camm [3], Göran Wettrell [6], Inger Fosdal [7], Michael Christiansen [4], Anders D. Børglum [1]

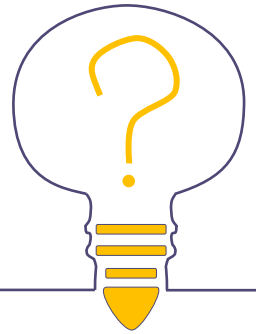
Calmodulin mutationer anno 2023

- 43 forskellige mutationer (sjældne).



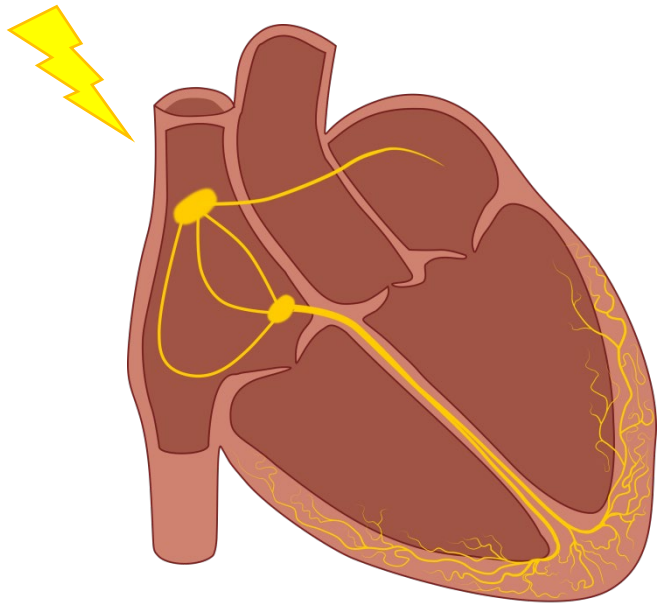
- Kun få videnskabelige eksperter i verden.

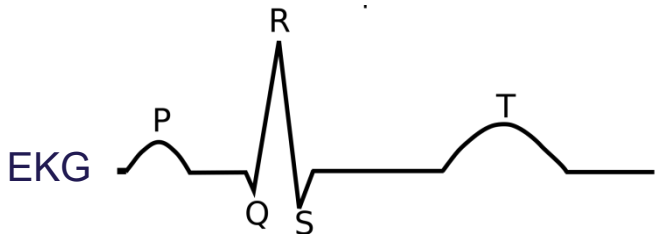
Hvordan forårsager calmodulin mutationer livsfarlige hjerterytmeforstyrrelser?



Hjertets funktion på organ-niveau

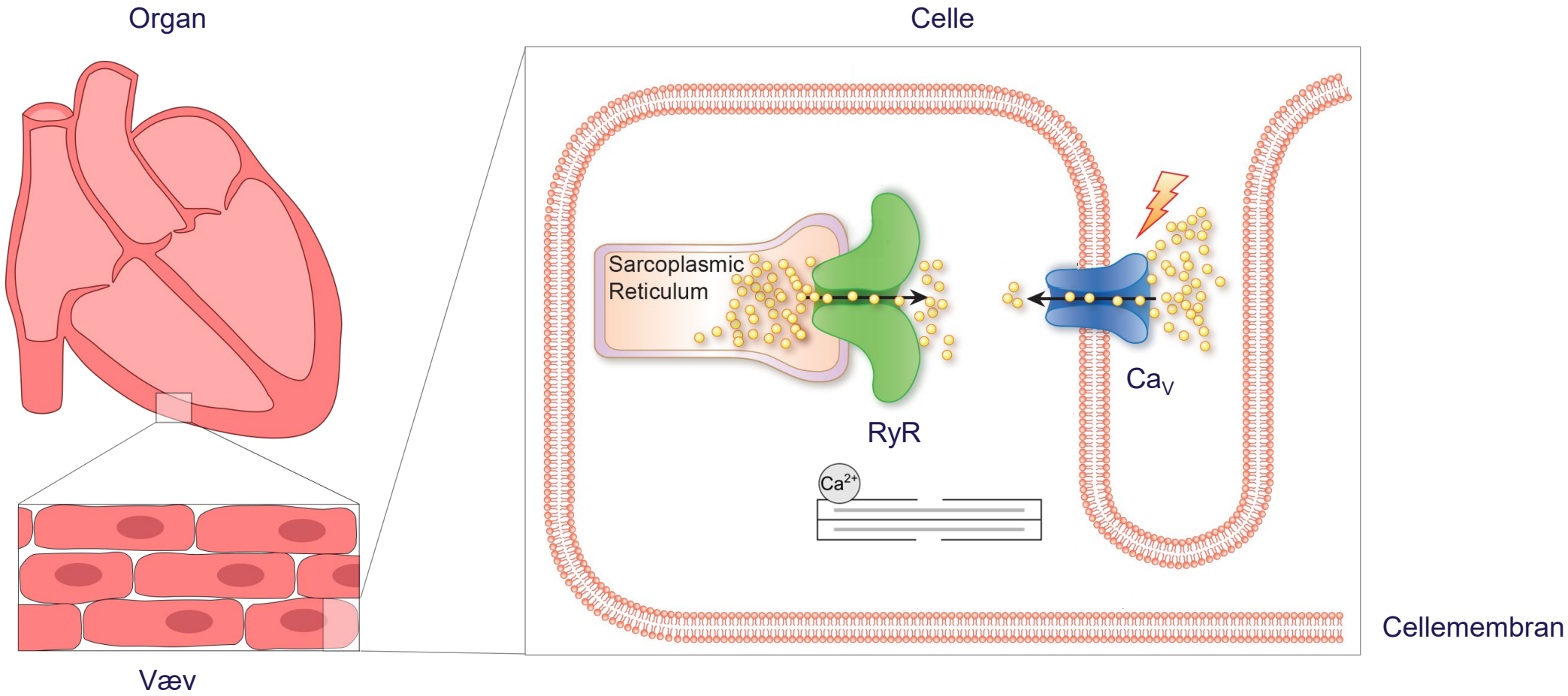
- Hjertet slår i respons på elektrisk stimuli
- De elektriske signaler forgrener sig til hjertets kamre som trækker sig sammen
- Sammentrækningen pumper blod ud i kroppen
- Elektroder udenpå kroppen kan måle de elektriske signaler (EKG)



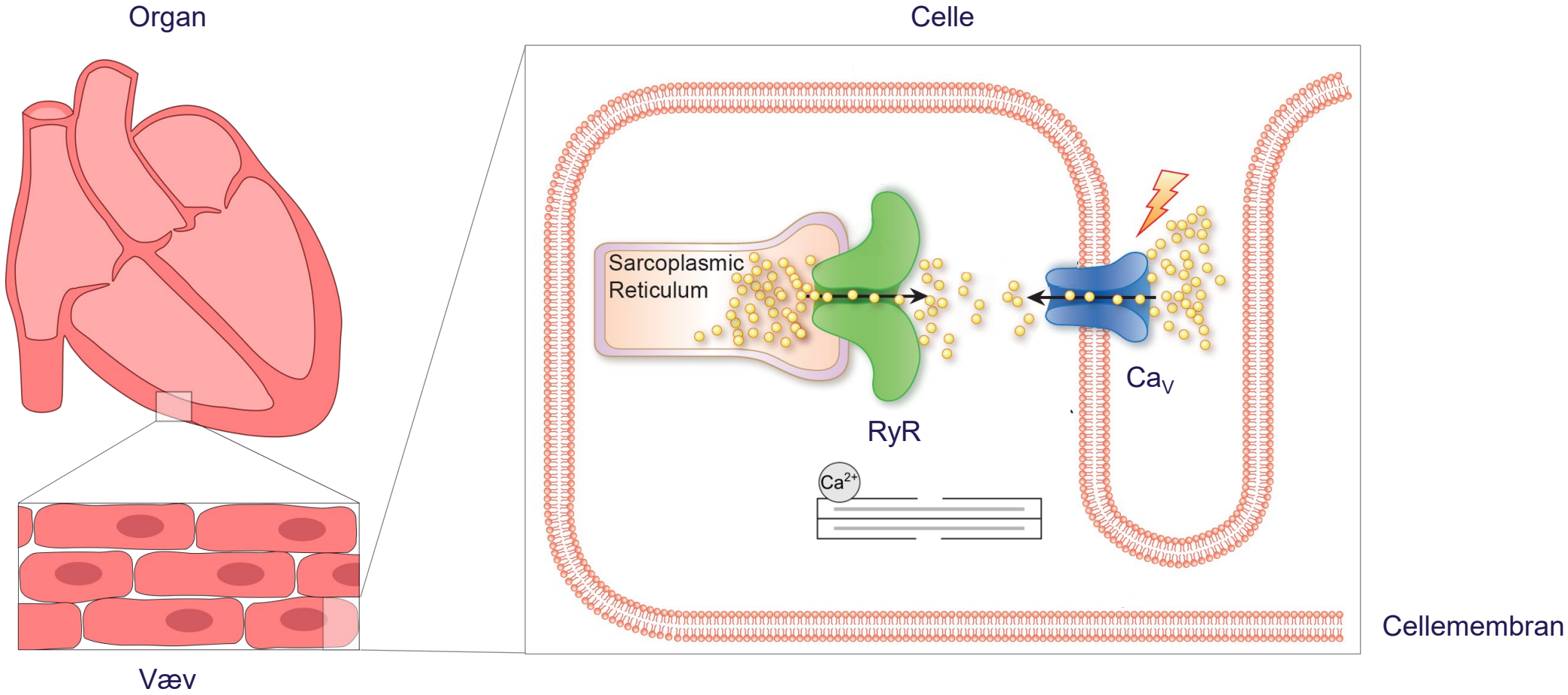


Elektro**K**ardio**G**ram (hjertediagram)

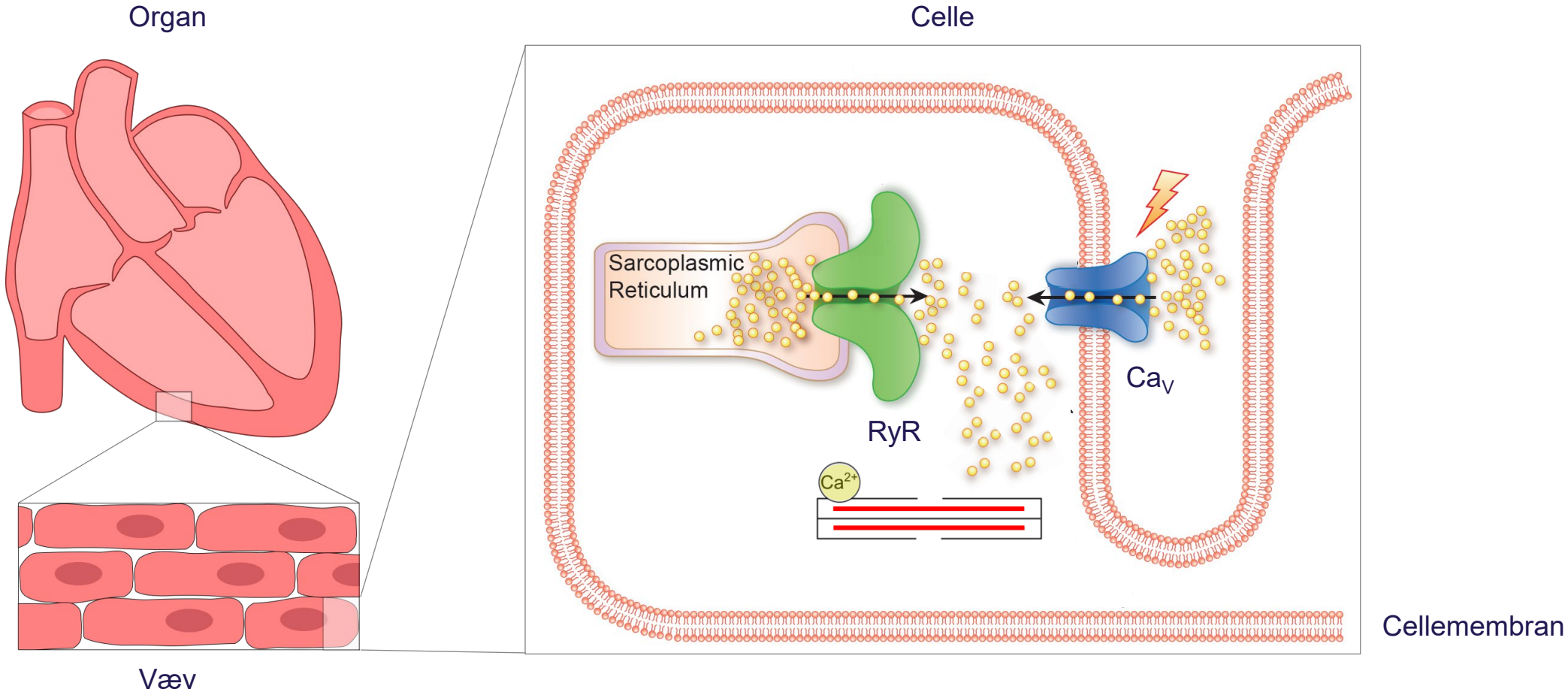
Calcium-ioner styrer et hjerteslag



Calcium-ioner styrer et hjerteslag

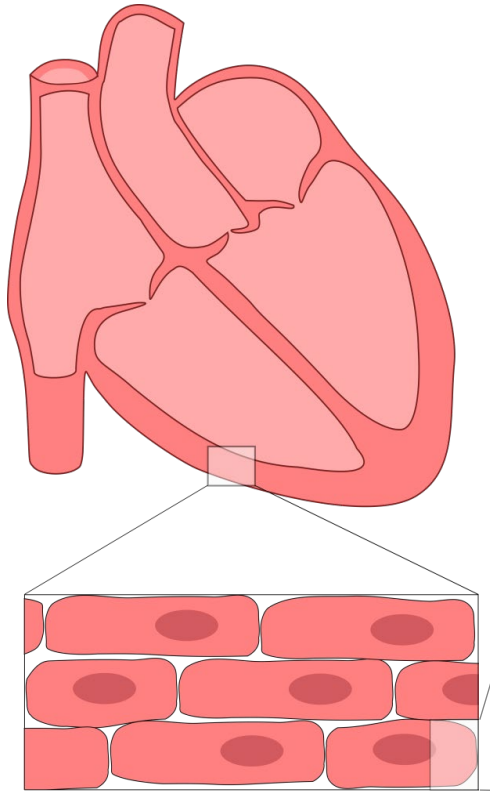


Calcium-ioner styrer et hjerteslag



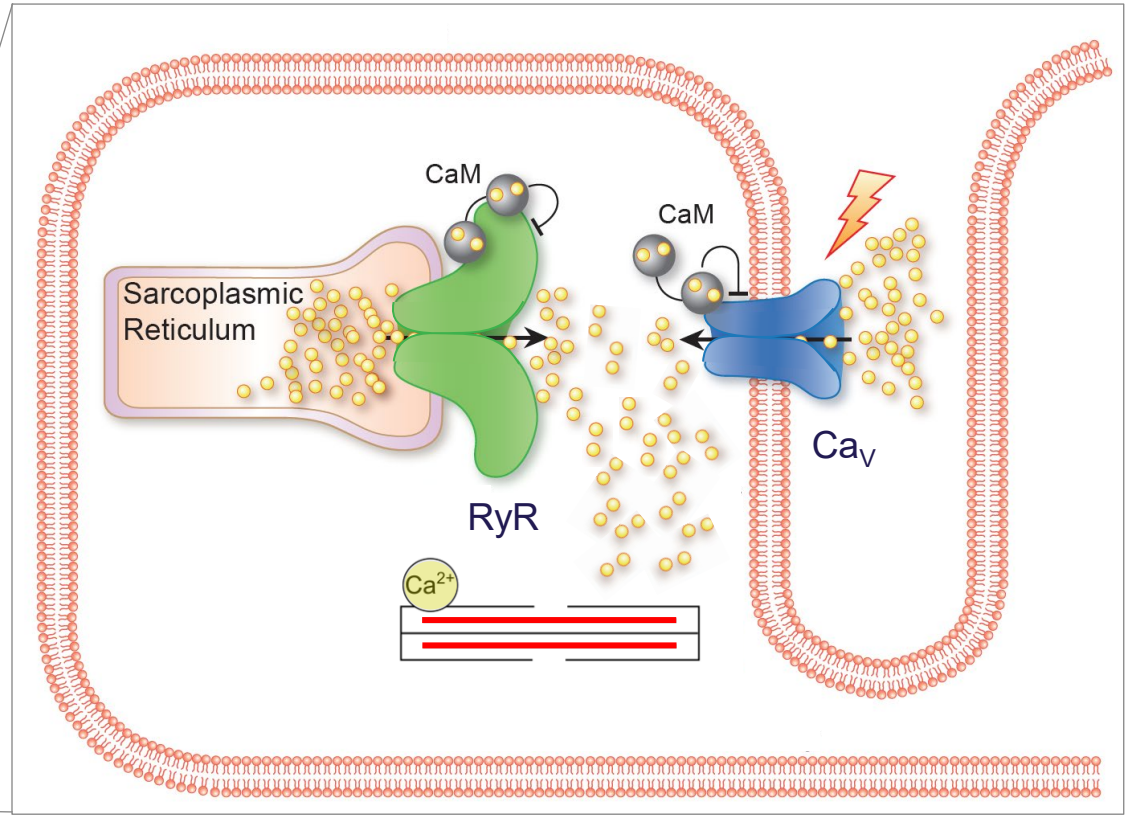
Calmodulins rolle i et hjerteslag

Organ



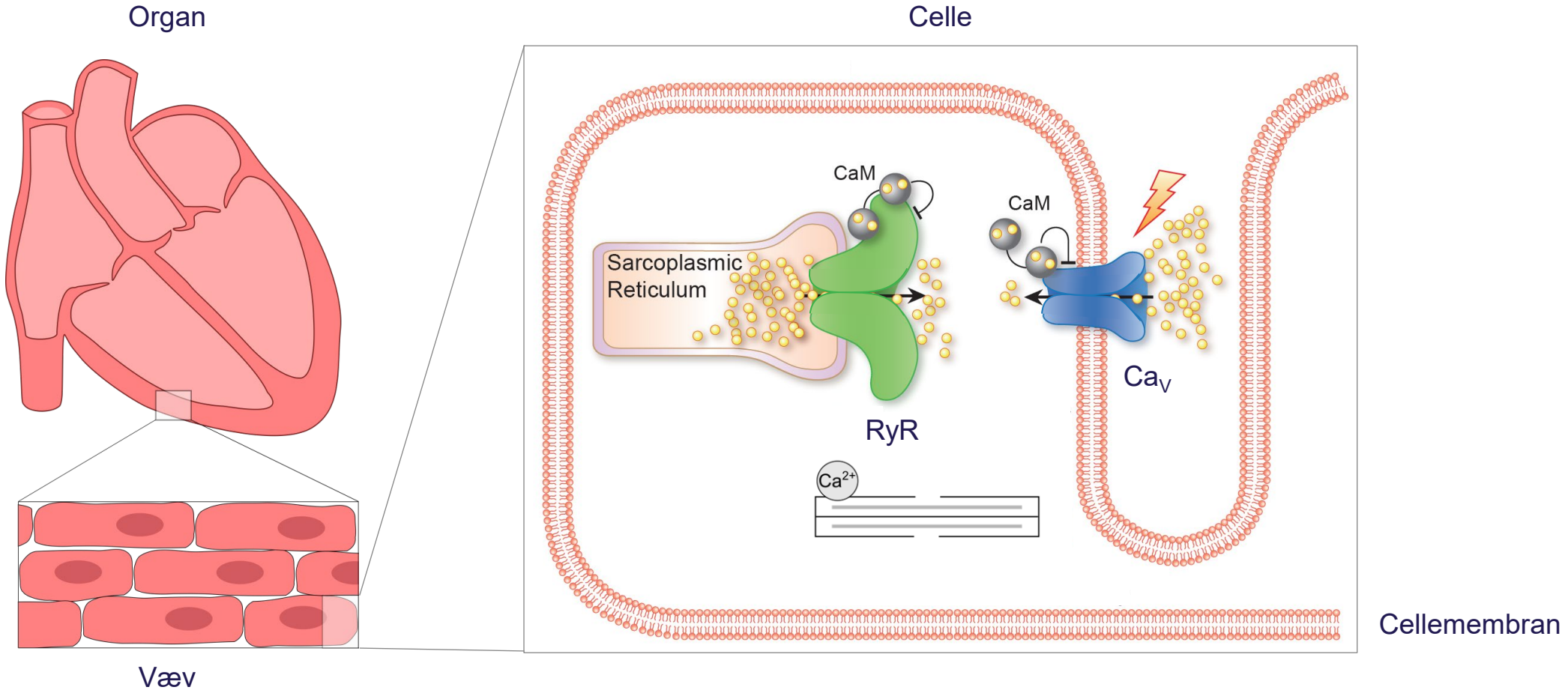
Væv

Celle

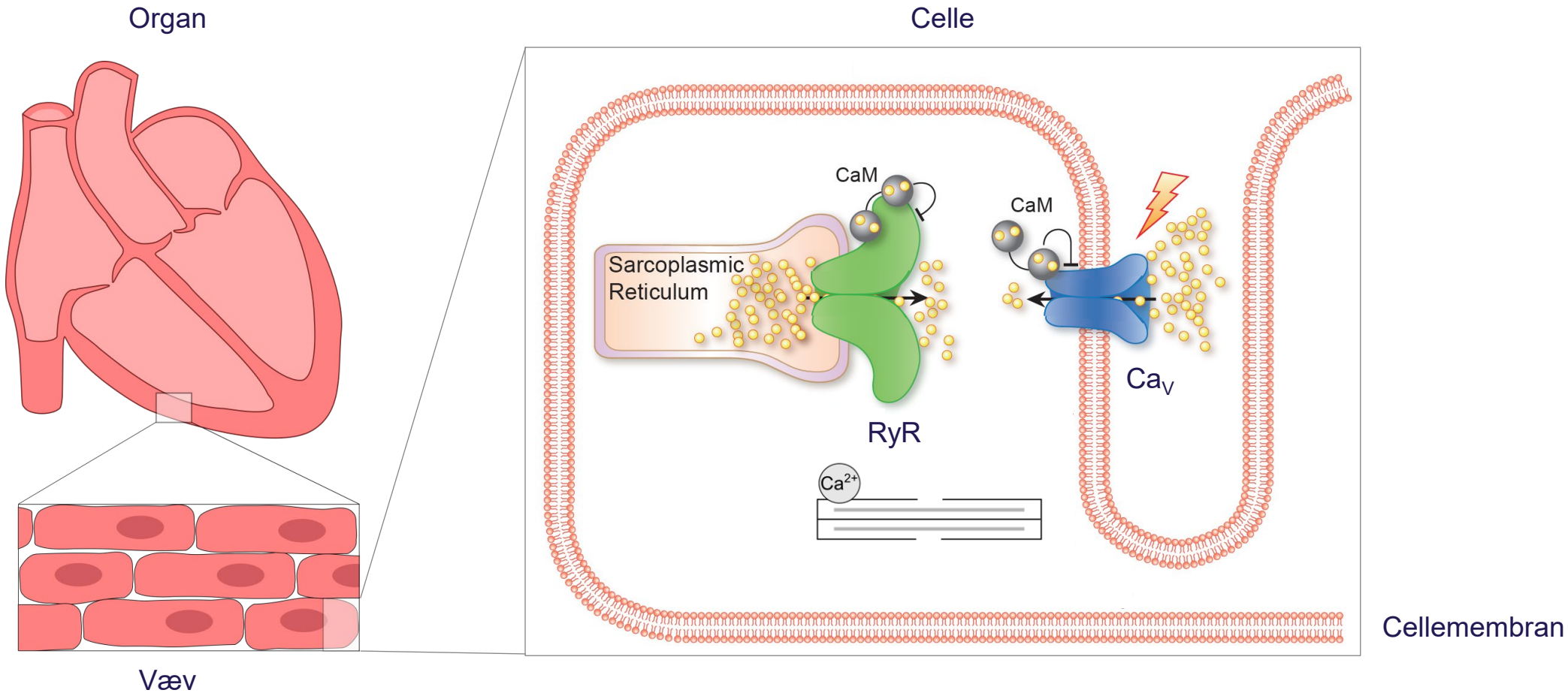


Cellemembran

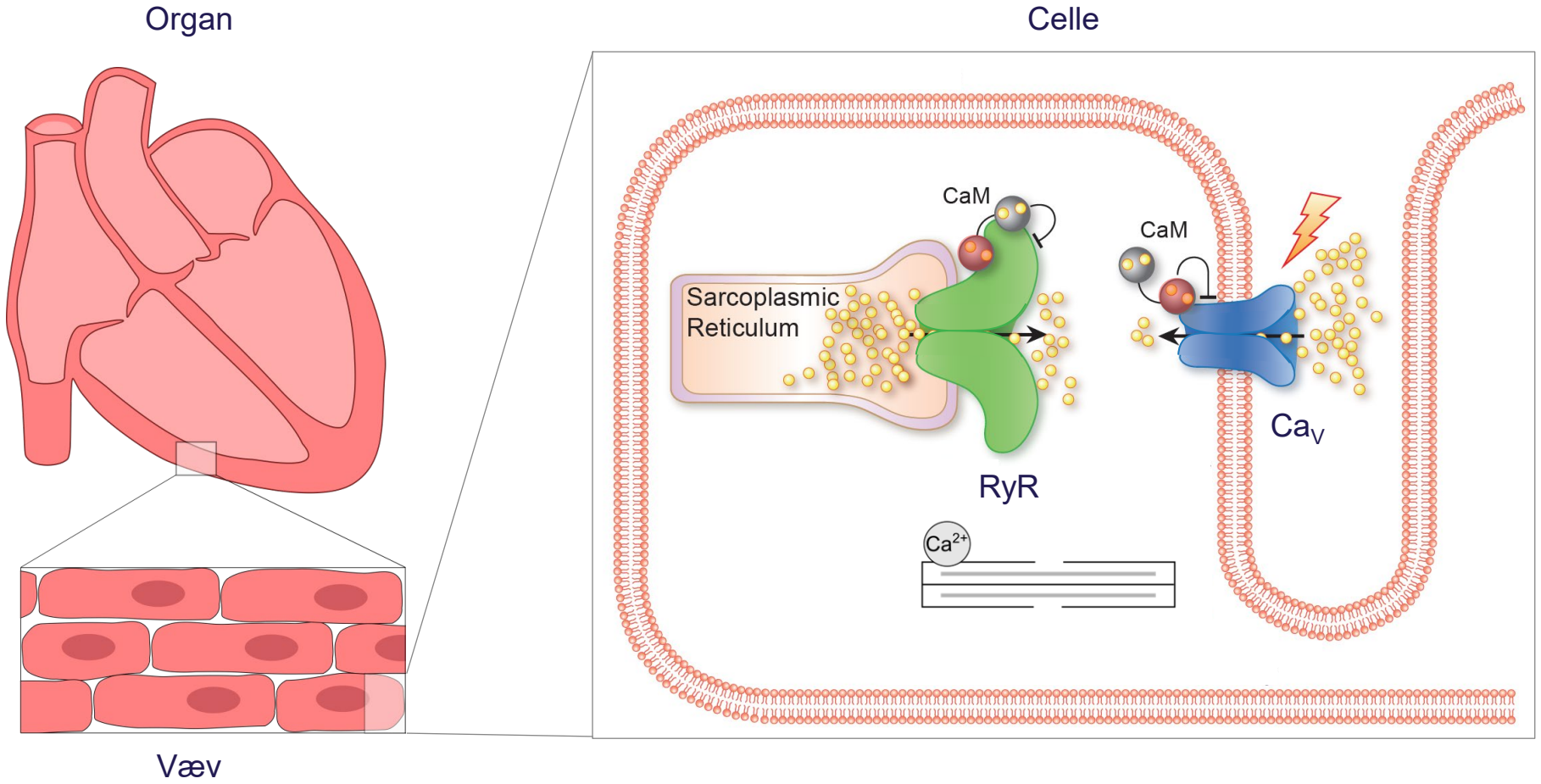
Calmodulins rolle i et hjerteslag



Mutationer i calmodulin fejlregulerer calcium-kanaler

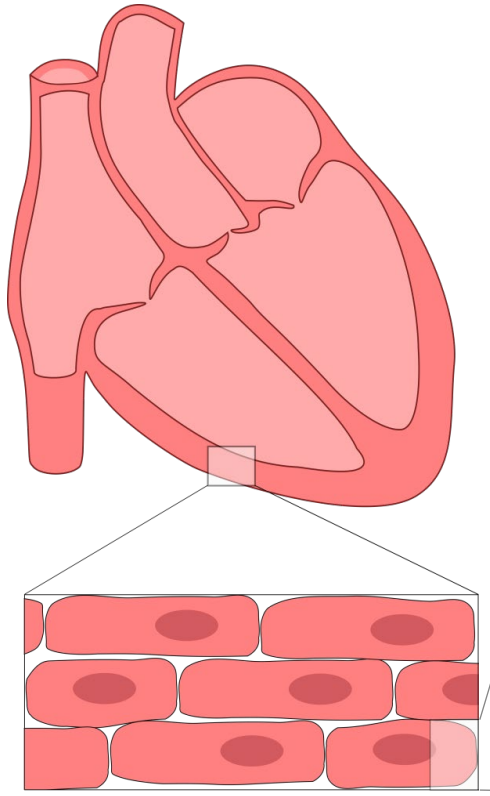


Mutationer i calmodulin fejlregulerer calcium-kanaler



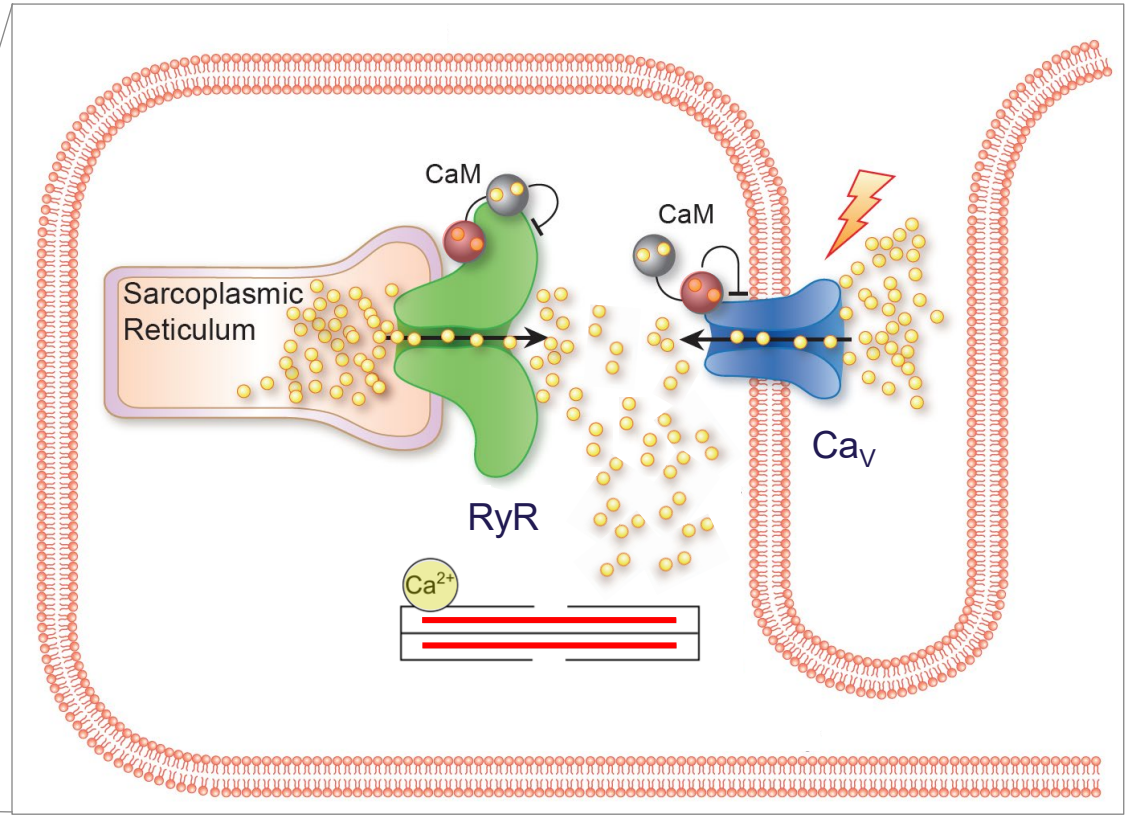
Mutationer i calmodulin fejlregulerer calcium-kanaler

Organ



Væv

Celle

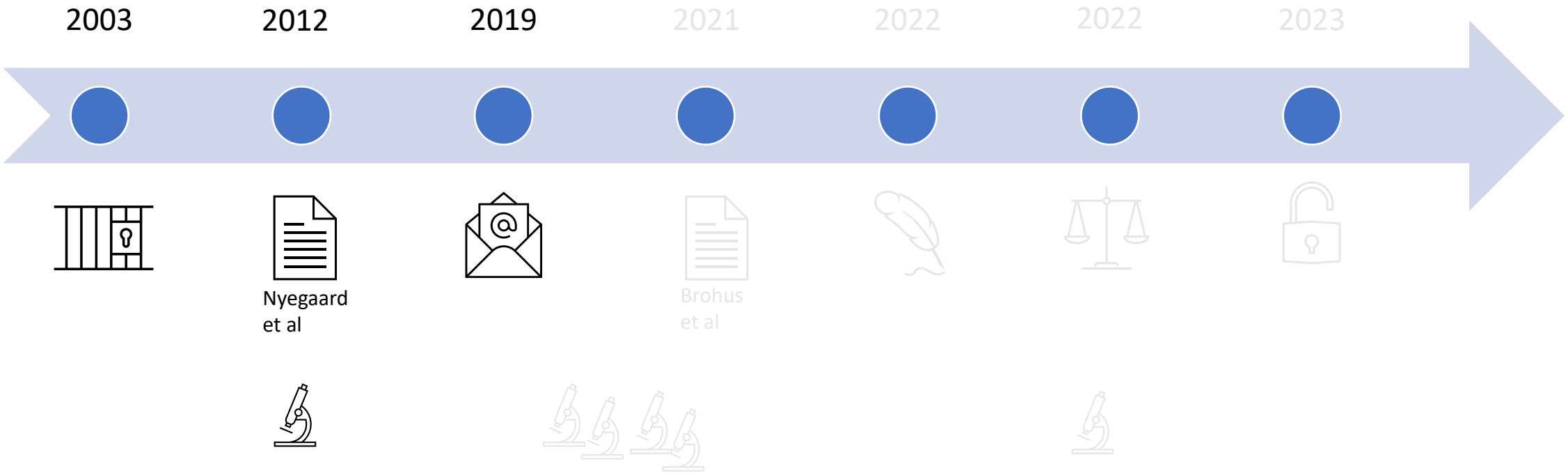


Cellemembran

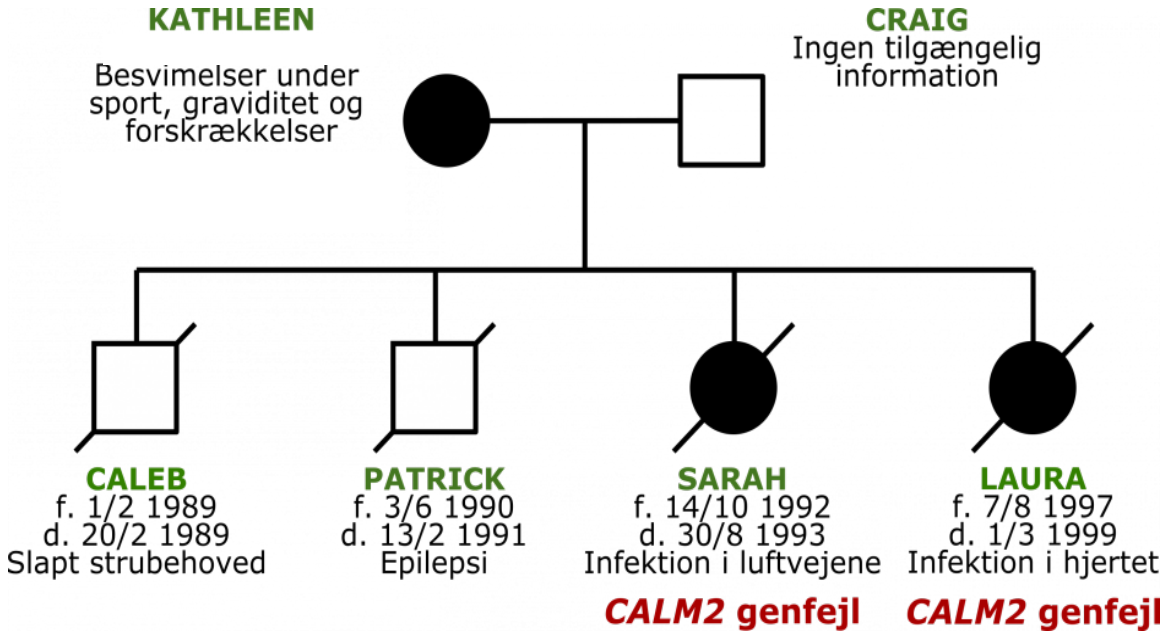
Mutationer i calmodulin giver hjertearrytmi ved at forstyrre calcium-signaler i hjertets celler.

Hvordan blev vi involveret i ‘Folbigg’ sagen?

1st Inquiry into the Folbigg Conviction



- 2015 Prof Steven Cordner:
  ”Ingen retsmedicinske beviser for at børnene er kvalt”
- 2018 Genetisk analyse af familien bestilles
- 2019 Inquiry (høring) into Folbigg conviction
  Nye retsmedicinske beviser
  Ney genetiske beviser



2019 - Høring efter den genetiske analyse

Prof Carola Vinuesa
Scientist

Prof Jonathan Skinner
Cardiologist

- Kathleen og de to døtre har farlig mutation in *CALM2* genet – *G114R*
- Mutationer i calmodulin-generne bliver brugt til at diagnostisere Hjerterytmeforstyrrelse og pludselig hjertedød
- Der er en anden famile med en *G114W* mutation (i stedet for *G114R*), hvor 2 børn døde af hjertestop

- Der er familier hvor nogle med en calmodulin mutation er mere alvorligt ramt end andre

- En calmodulin mutation af denne type og på dette sted er aldrig set før – så vi kan ikke konkludere at den er farlig

- Men hvorfor er Kathleen så ikke død af t hjertestop?

- Der er ingen rapporter der beskriver helt unge børn med calmodulin mutationer som dør mens de sover

Juli 2019

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Kathleen Folbigg inquiry into her four convictions reinforces her guilt, judge finds

By Nick Sas

Posted Mon 22 Jul 2019 at 12:04pm, updated Tue 23 Jul 2019 at 2:40am

Novel likely pathogenic CALM2 mutan...

Filer Meddelelse Hjælp Acrobat Fortæl mig, hvad du vil foretage dig

Søg

Novel likely pathogenic CALM2 mutant in legal case

CG

Carola Garcia de Vinuesa <carola.vinuesa@anu.edu.

Til Michael Toft Overgaard

28-06-2019

Opfølgning. Fuldført den 11. juli 2019.
Du svarede på denne meddelelse den 16-04-2021 11:20.

Crotti Eur Heart J 2019.pdf
949 KB

Dear Michael,

I have recently been involved in an inquiry into the Folbigg case. Kathleen Folbigg was accused of murdering her 4 children and has been in jail for 15 years. There are several documentaries online about her case.

I was asked to provide a genetic report on the family (WGS/WES of 4 deceased infants and mother). We found a variant in CALM2 (G114R) in 2 of the children inherited from the mother, which Prof Peter Schwartz believes it is likely pathogenic (I can provide you with his report if needed). It resides in the same calmodulin residue as the one found in another family (CALM3 G114W) in which the proband and brother died of IVF-SCD at ages 4 and 5 (See attached Crotty et al). The variant was inherited from an asymptomatic mother that was a mosaic.

I have ben adviced by Alfred George that you are the best person to approach regarding functional assay of the CALM2 variant. This evidence would be invaluable in court if the appeal is successful and would be included in a scientific publication of this extraordinary case.

I really hope you can help us get to the bottom of this case.

Kind regards,

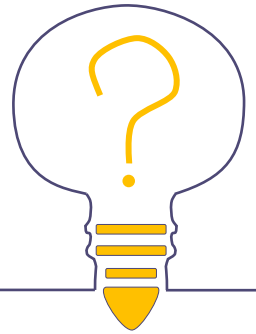
Carola

P.S. Here is a link to our initial report, available online:
https://www.folbigginquiry.justice.nsw.gov.au/Documents/Amended%20Exhibit%20AF%20-%20Joint%20report%20of%20Canberra%20genetics%20team%20dated%2029%20March%202019.pdf
For info on CALM2 mutation, see pages 20-22

”Jeg håber virkelig du kan hjælpe os med at komme til bunds i denne sag”

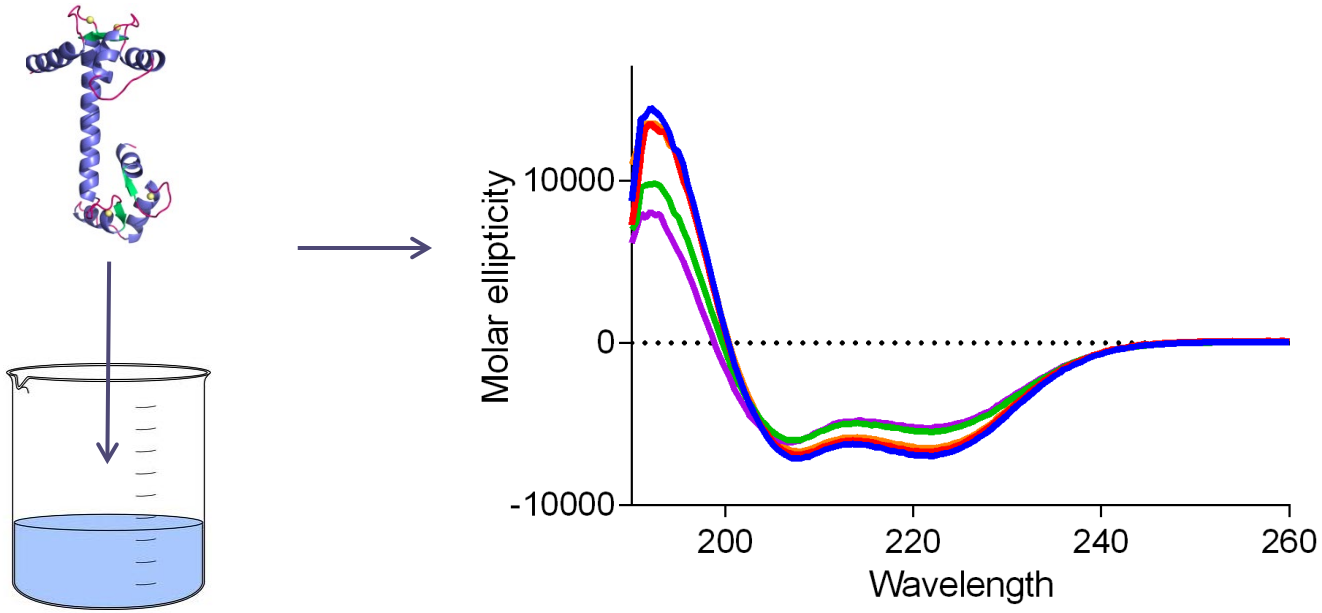
”Selvfølgelig kan jeg hjælpe!!”

Ændrer Folbigg mutationen calmodulins funktion i hjertet og kan den have forårsaget børnenes død?

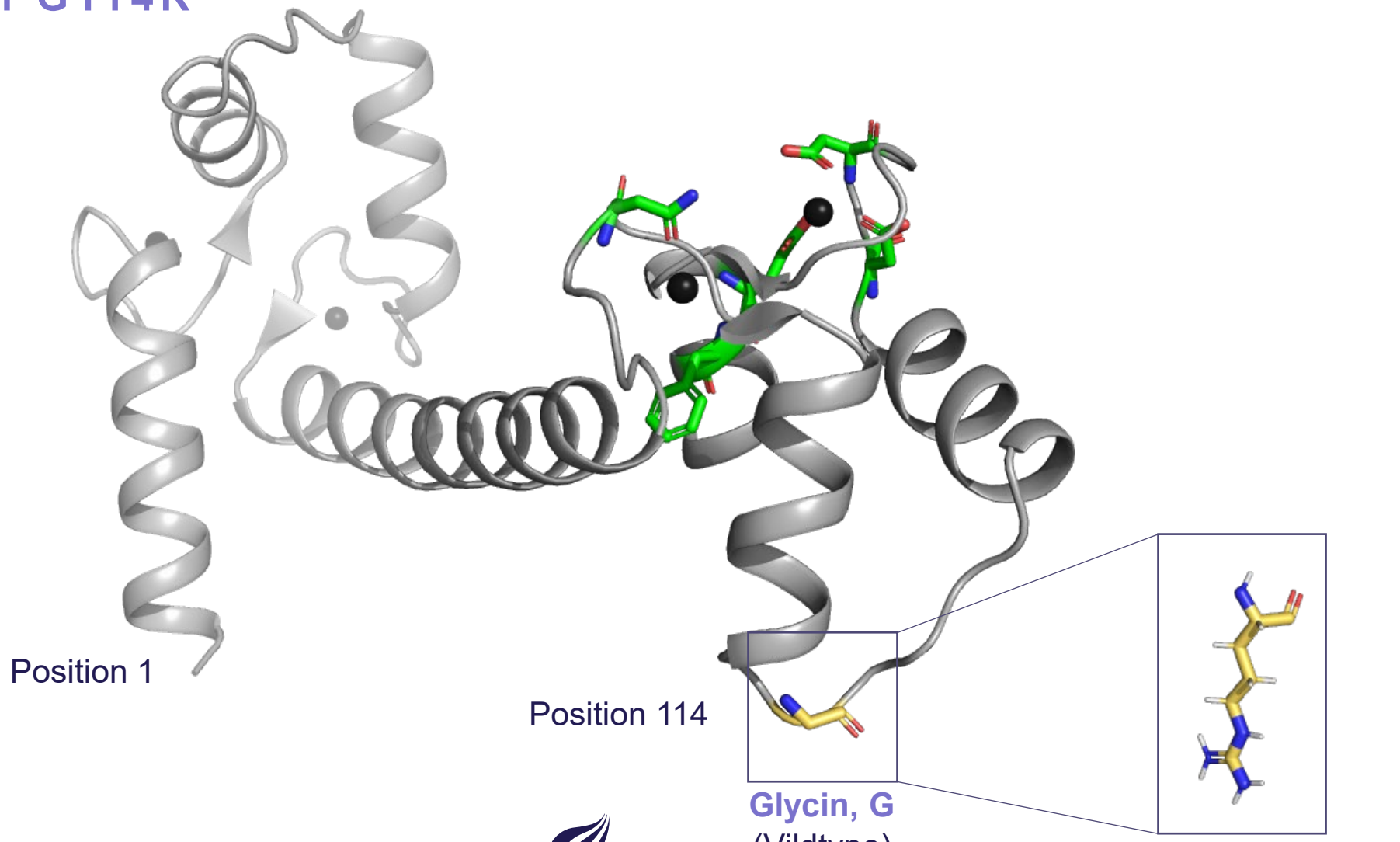


Biofysiske metoder kan studere proteiner i et isoleret miljø (udenfor cellerne)

- Producer og oprens protein
- Opbevar i buffer/opløsning
- Mål på:
  - Størrelse
  - Struktur
  - Vekselvirkninger
  - Aktivitet



Hvor og hvad er mutationen?
– calmodulin G114R



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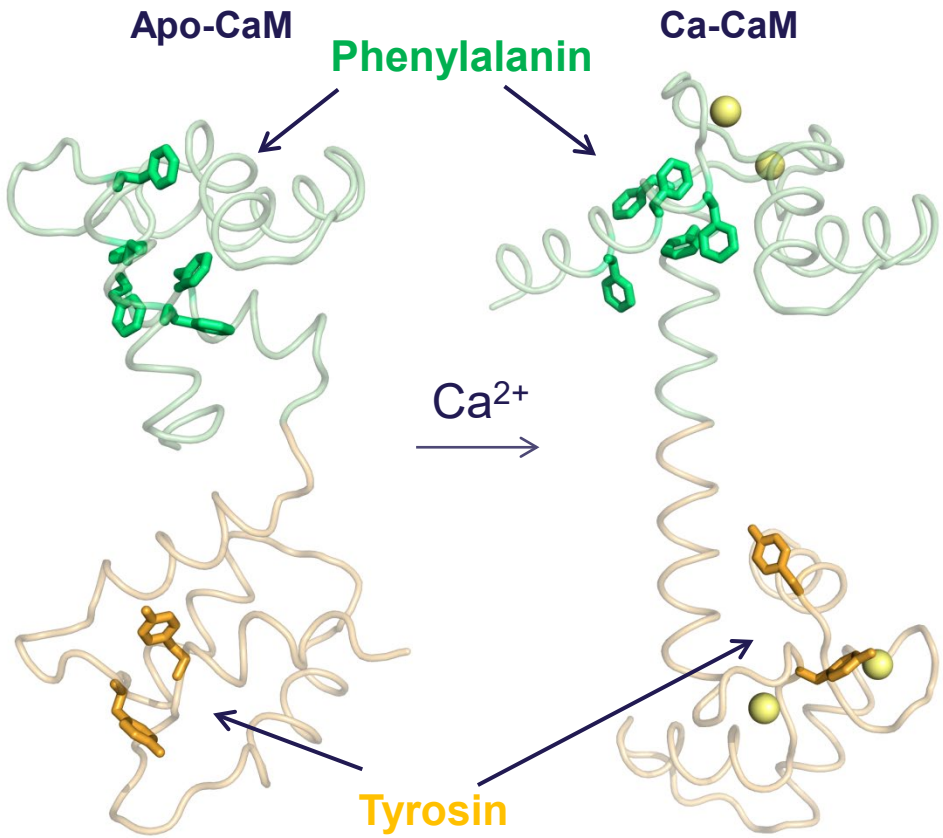
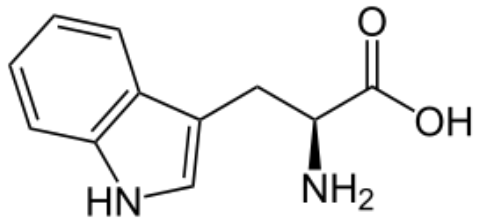
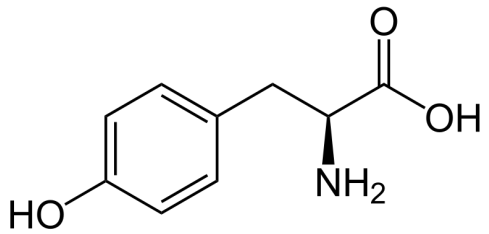
Måling af calmodulins evne til at binde calcium
– fluorescens spektroskopi

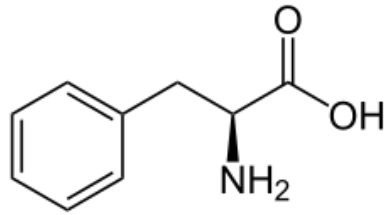




Tryptofan

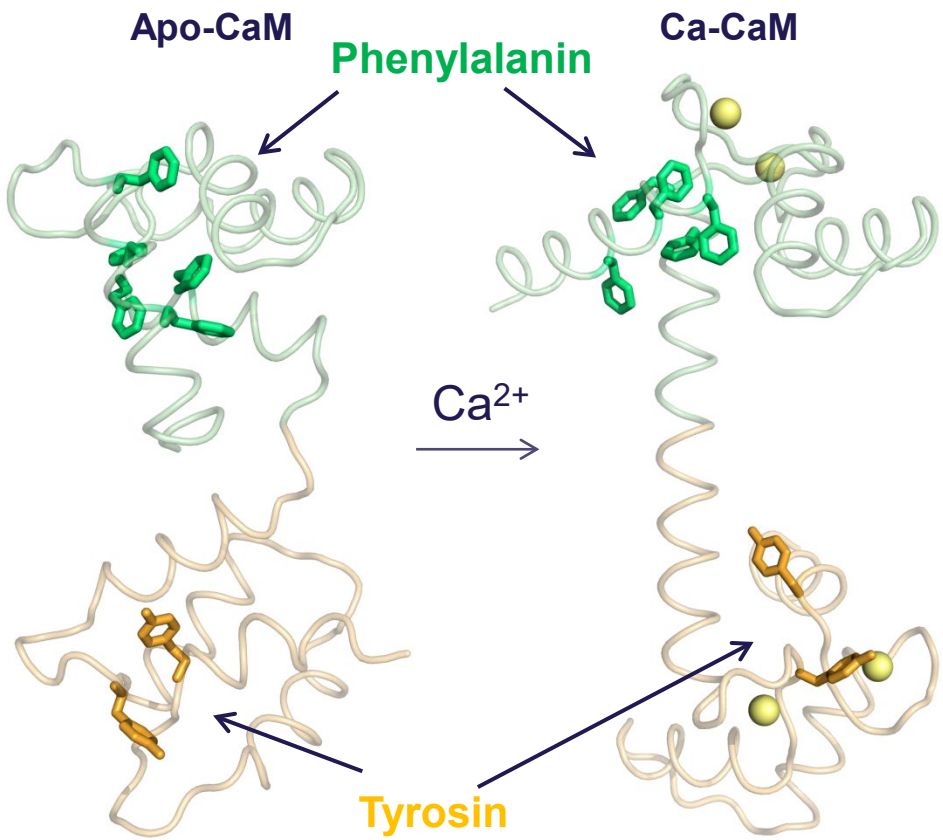


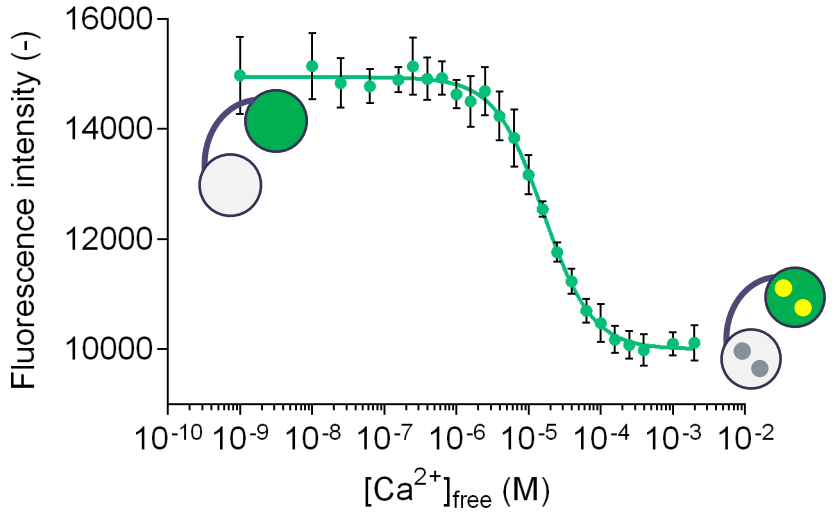
Tyrosin

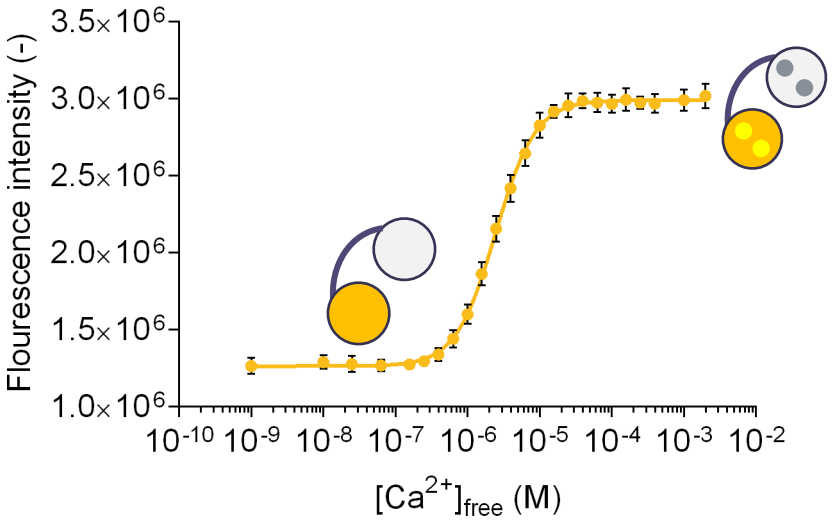


Phenylalanin

Måling af calmodulins evne til at binde calcium
– fluorescens spektroskopi







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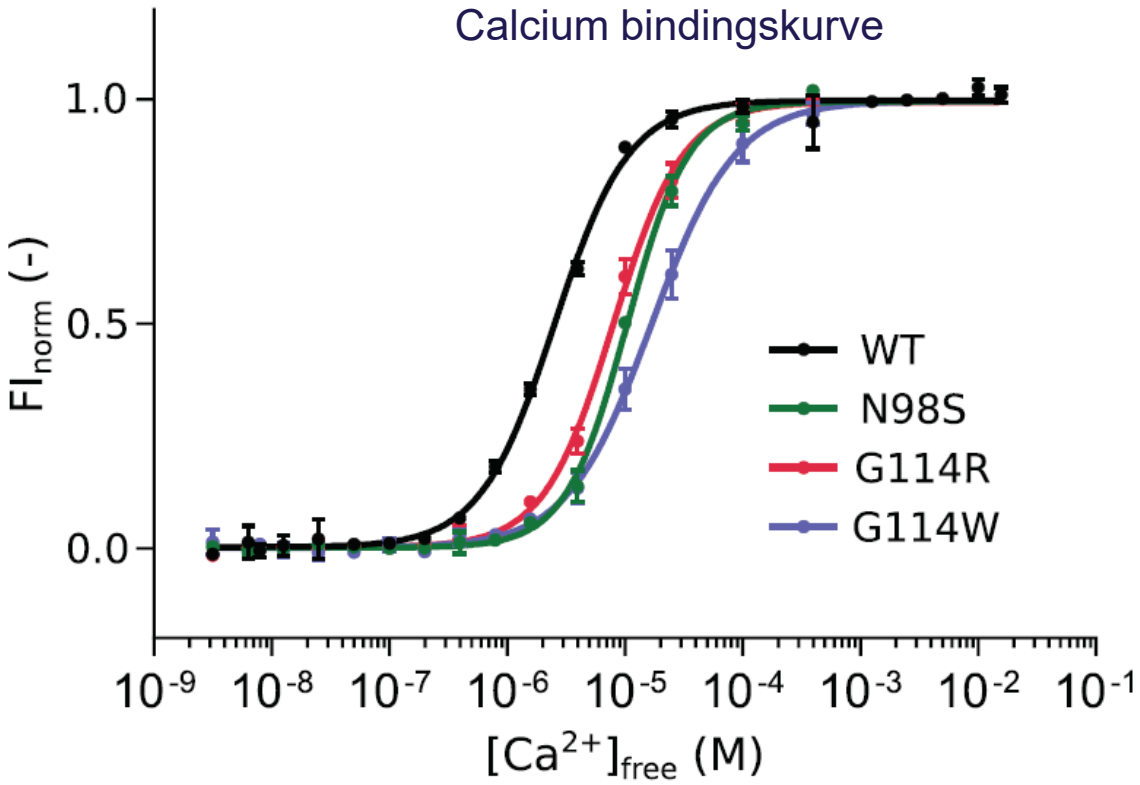
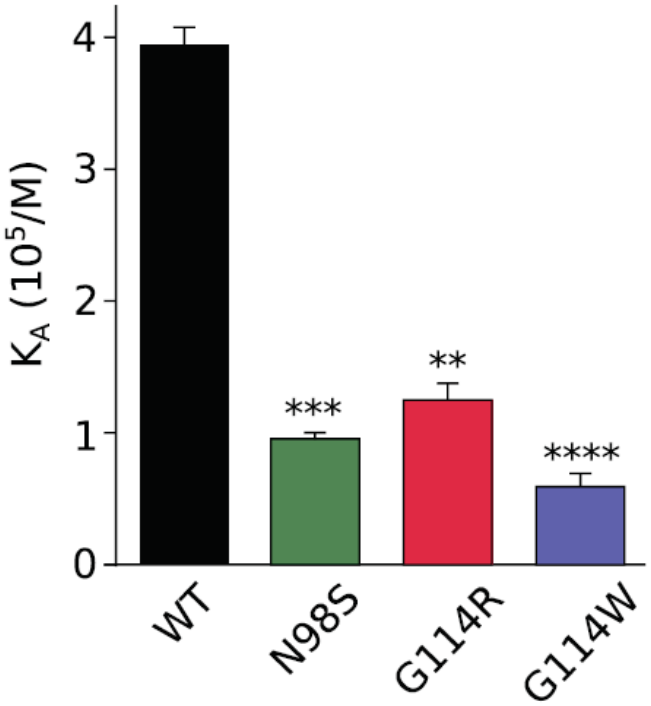
Folbigg mutationen forringer calmodulins evne til at binde calcium

Calcium bindingskurve



Bindingsstyrke



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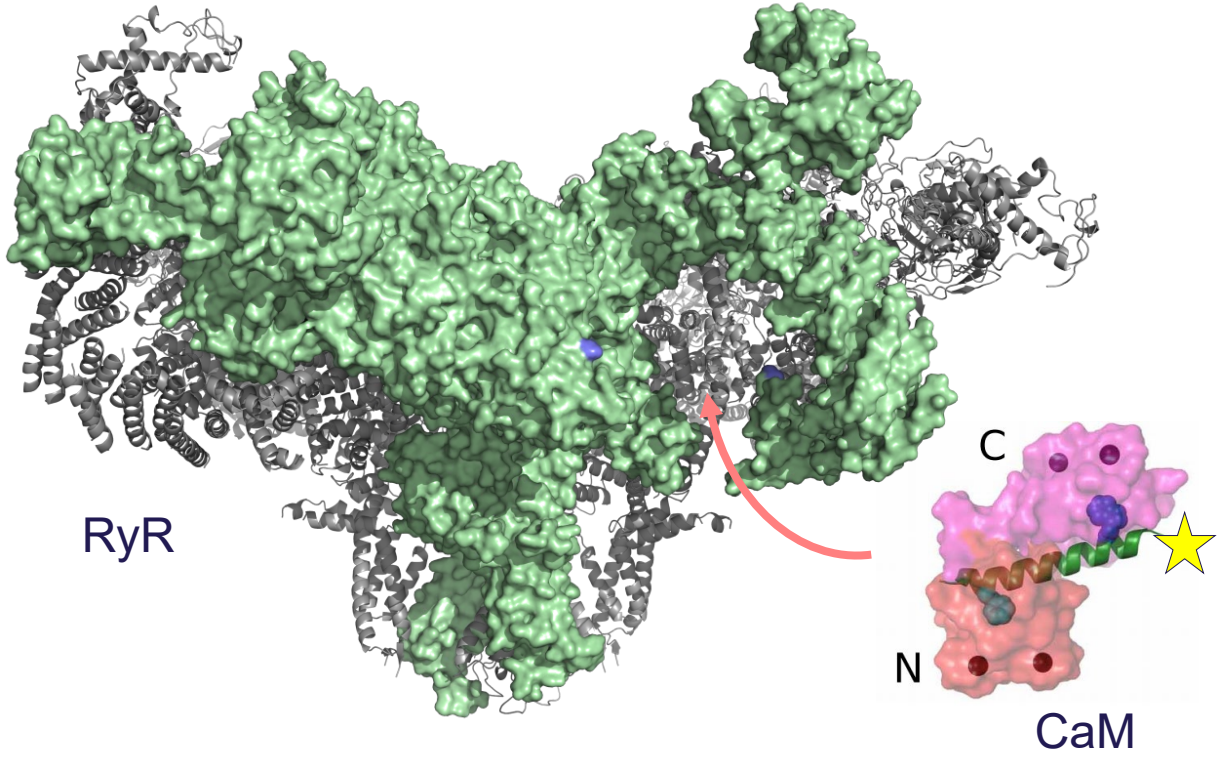
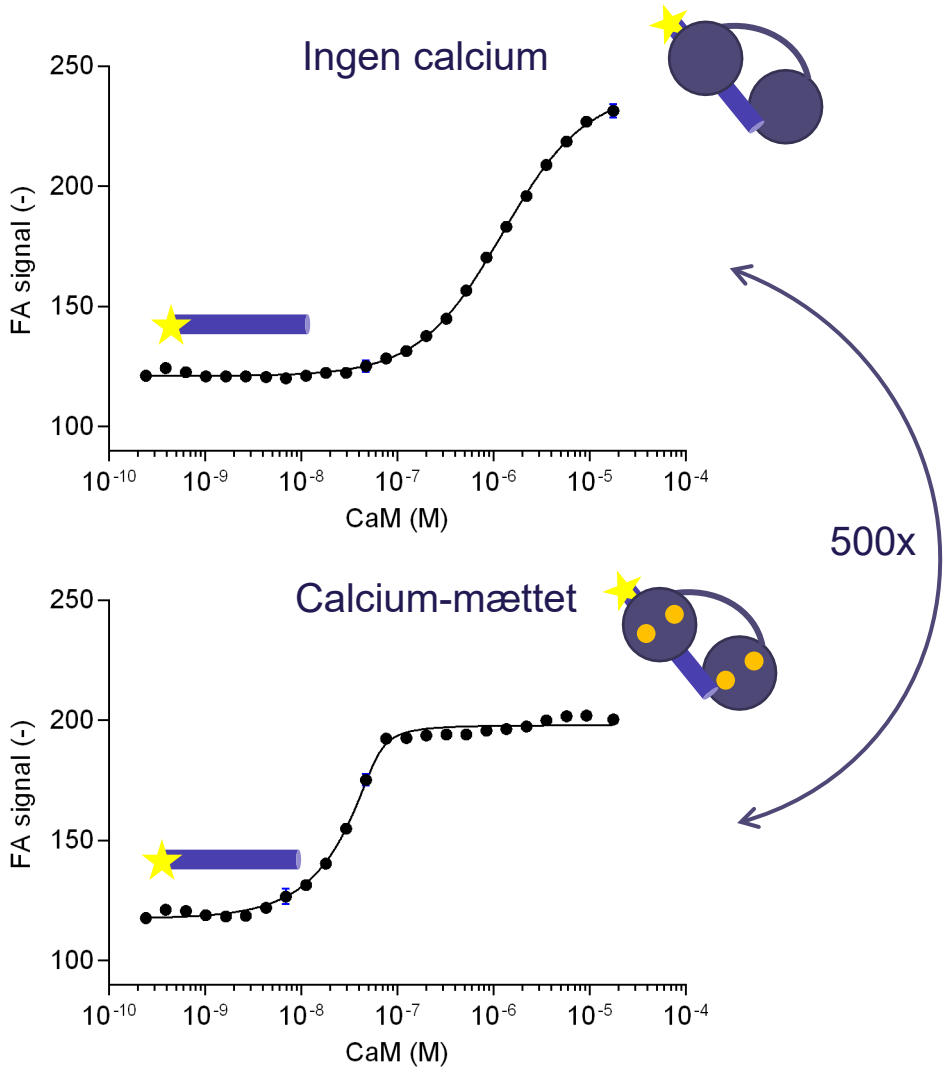
Måling af calmodulins evne til at vekselvirke med calcium-kanaler – fluorescens anisotropi





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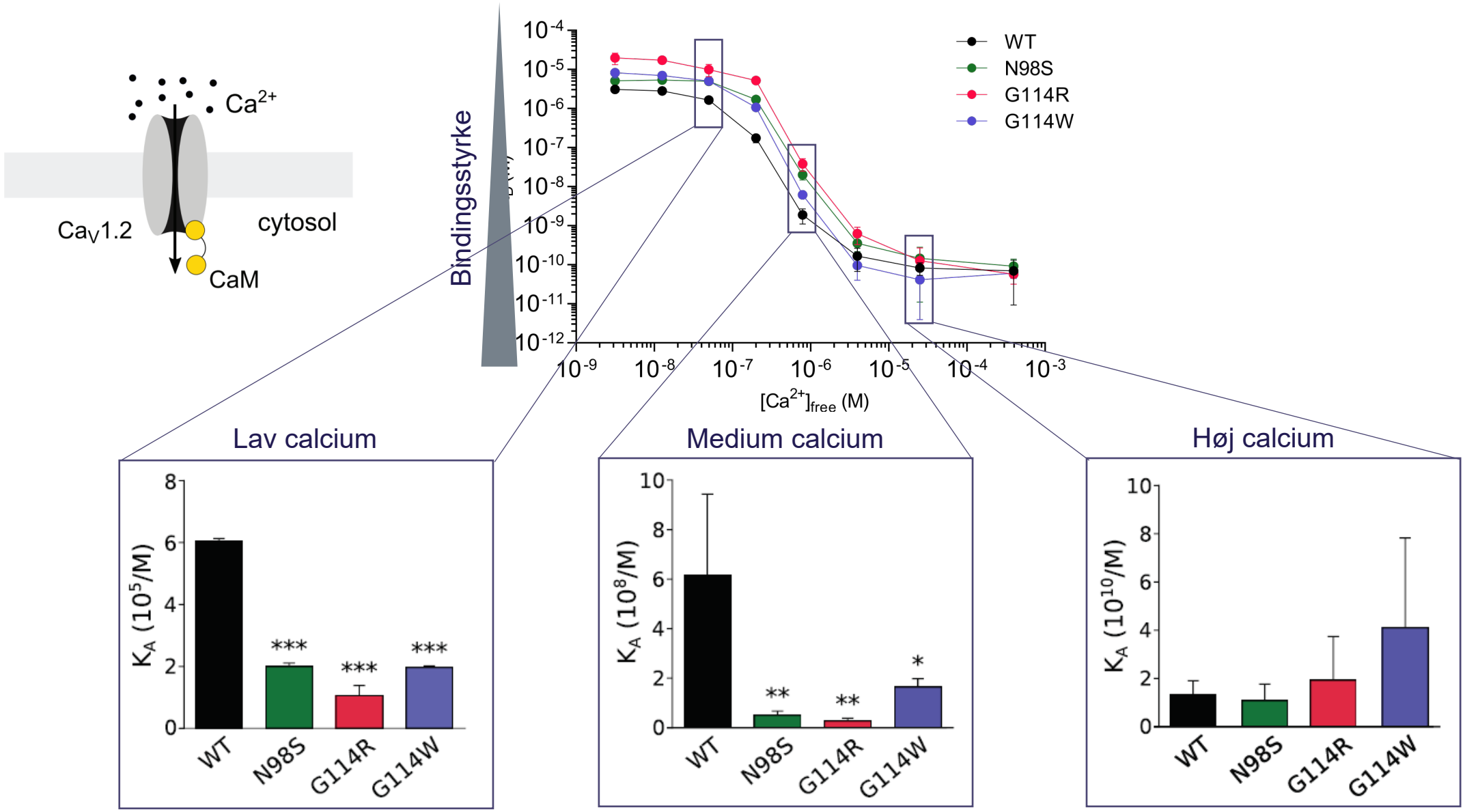
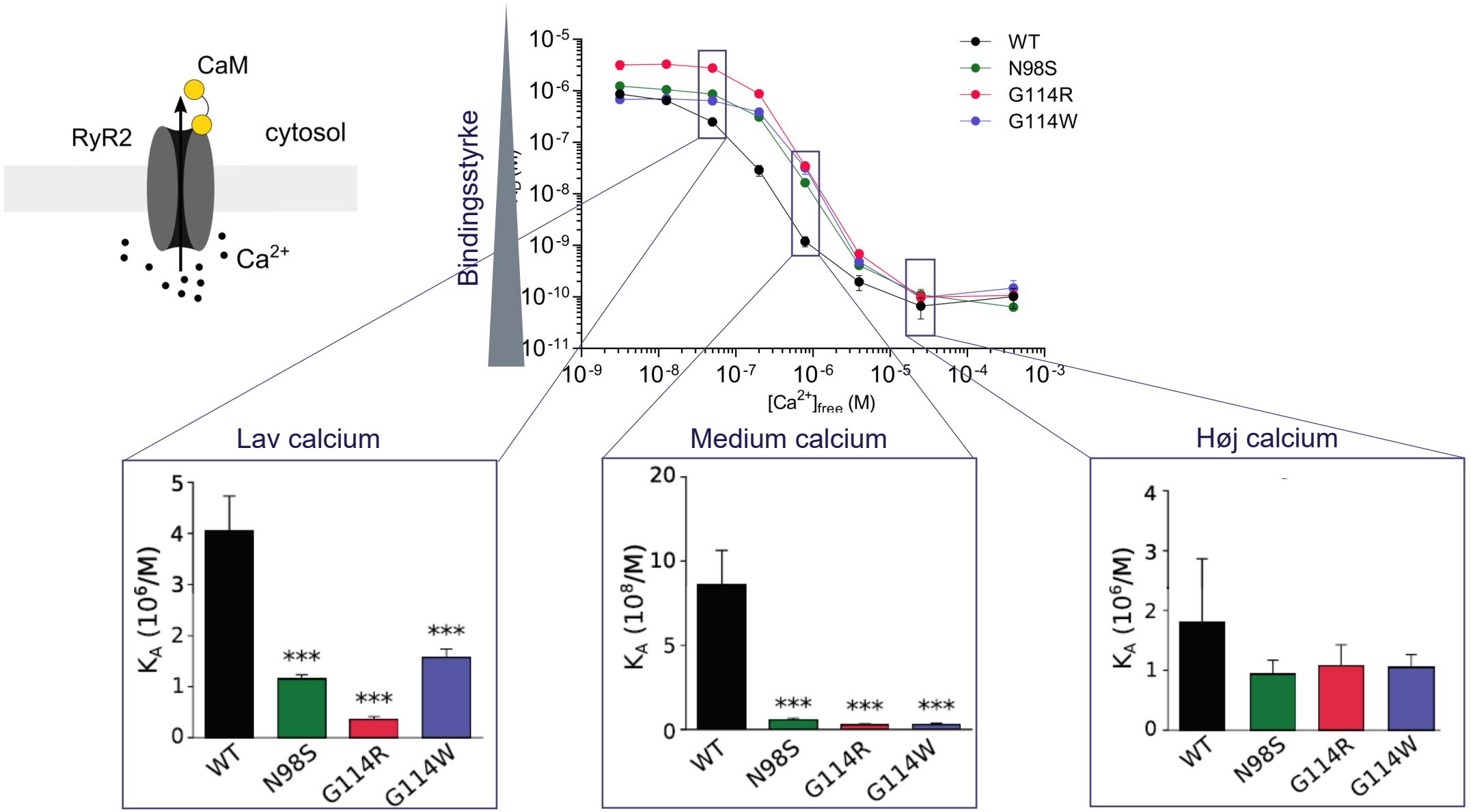
Folbigg mutationen forringer calmodulins evne til at binde til $Ca_V1.2$

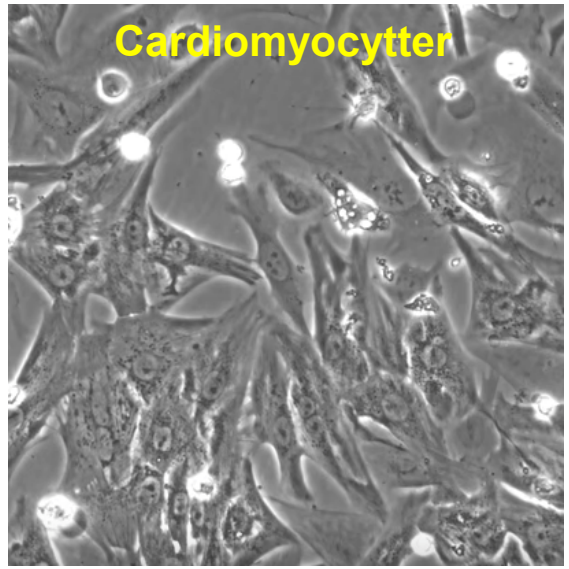


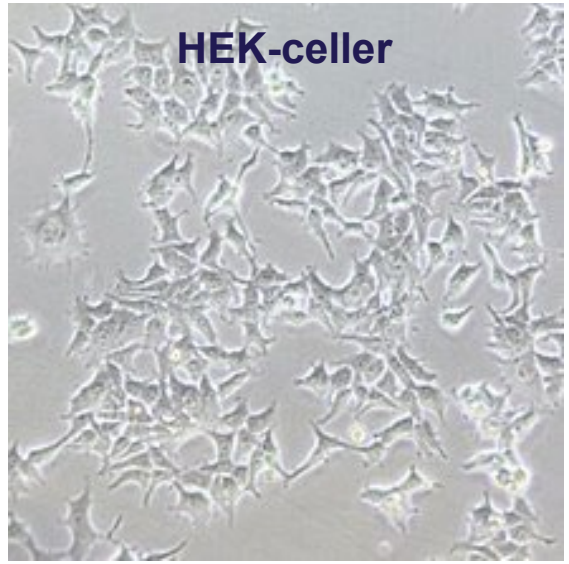
Folbigg mutationen forringer calmodulins evne til at binde til RyR2



Cellekulturer kan bruges til at studere (komplekse) effekter

- Isolér specifik celletype *eller* anvend standardiseret cellelinje
- Stimulér/påvirk cellerne
- Mål på:
  - Sundhed (viabilitet, motolitet)
  - Signalering (on/off)
  - Enzymaktivitet
  - Transportaktivitet (fx. Ca^{2+}-strømninger)





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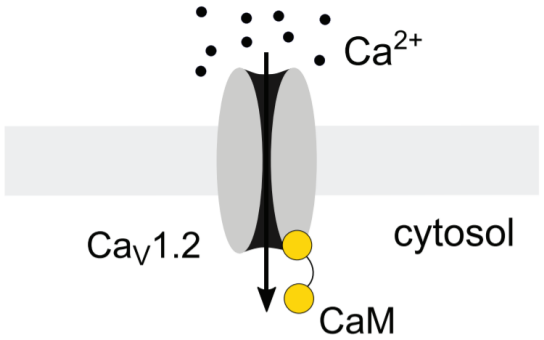
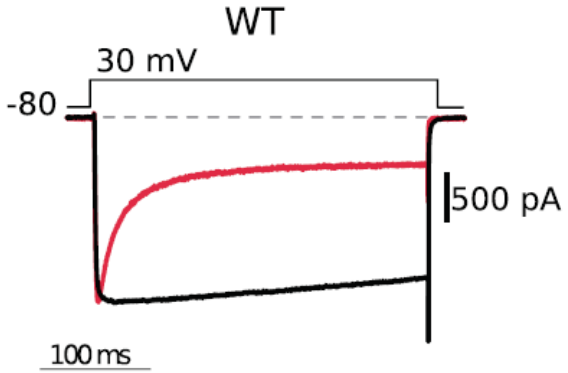
Folbigg mutationen forringer calmodulins evne til at lukke $Ca_V1.2$





Ivy Dick
(USA)

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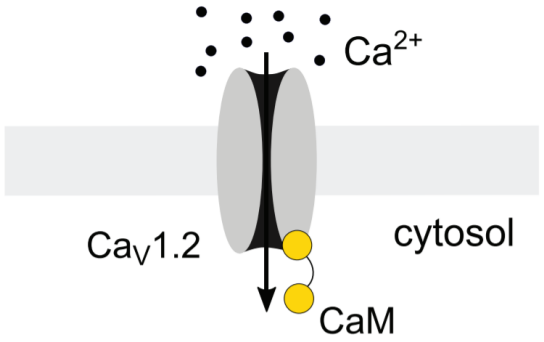
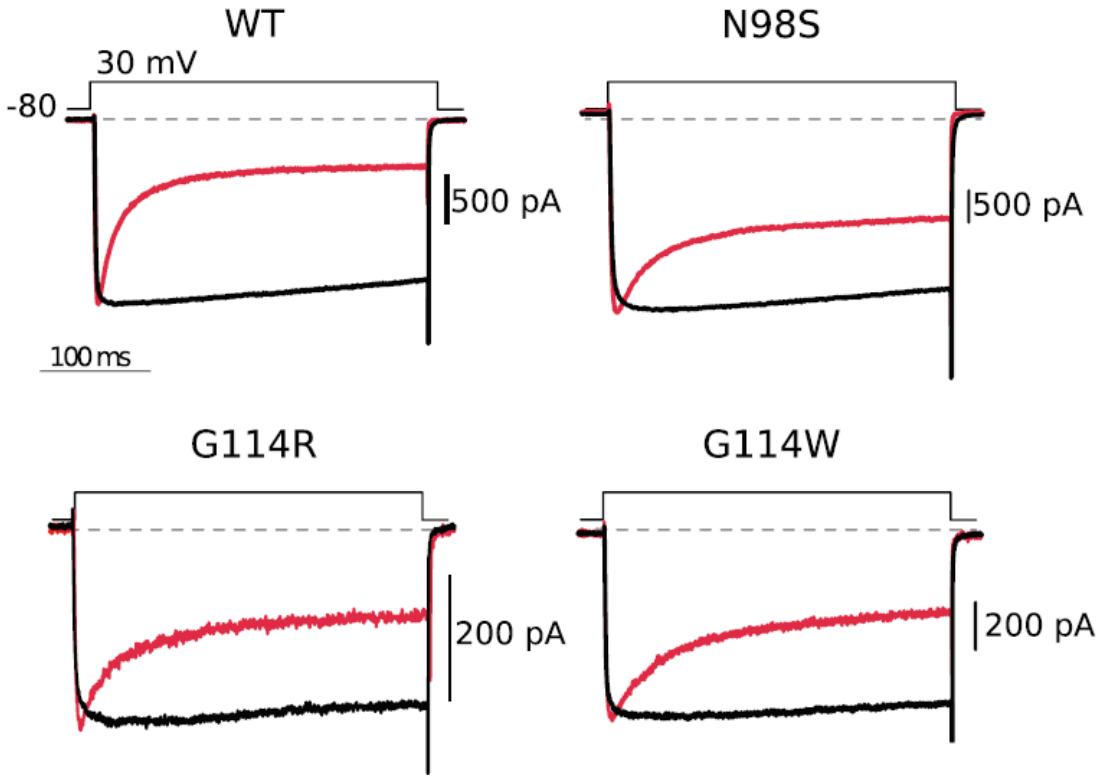
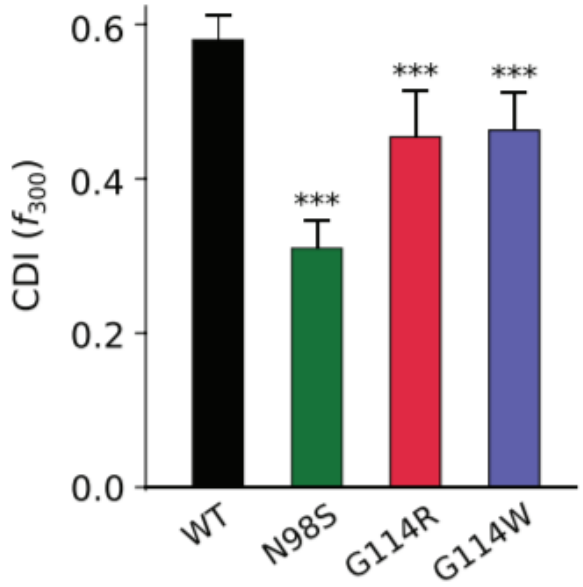
Folbigg mutationen forringer calmodulins evne til at lukke $Ca_V1.2$







Ivy Dick
(USA)

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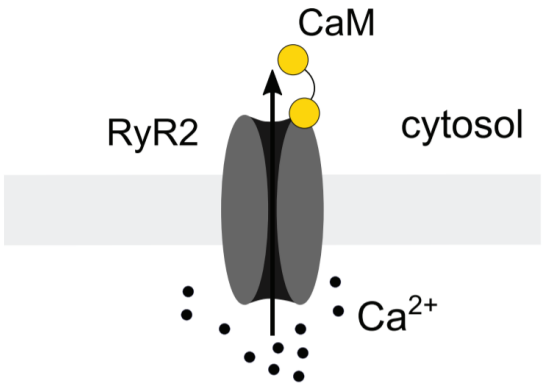
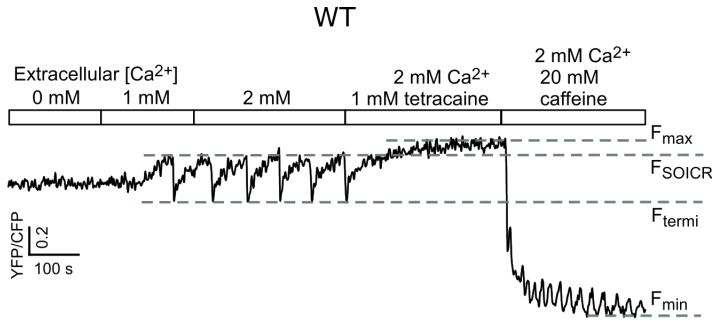
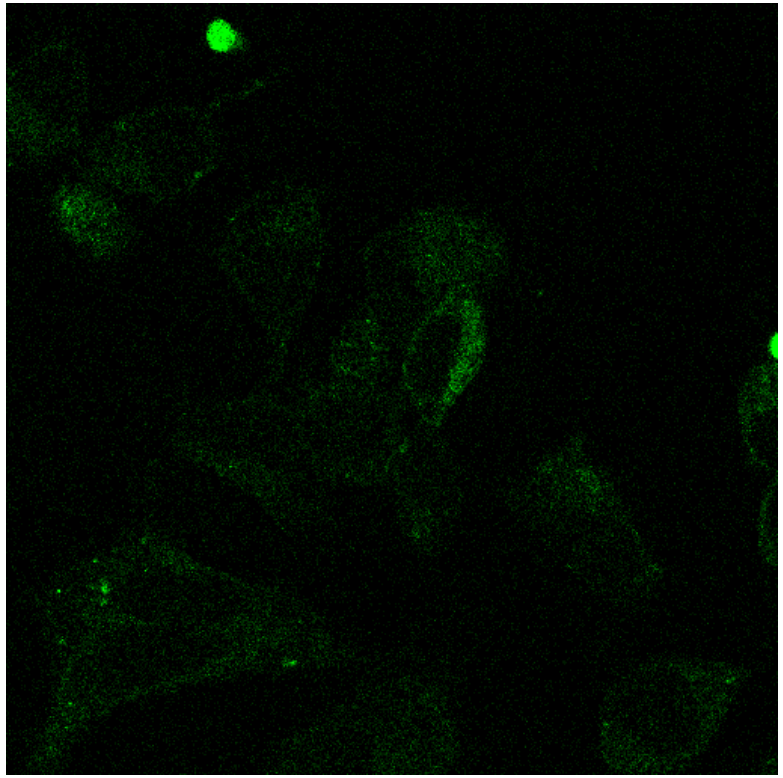
Folbigg mutationen forringer calmodulins evne til at lukke RyR2

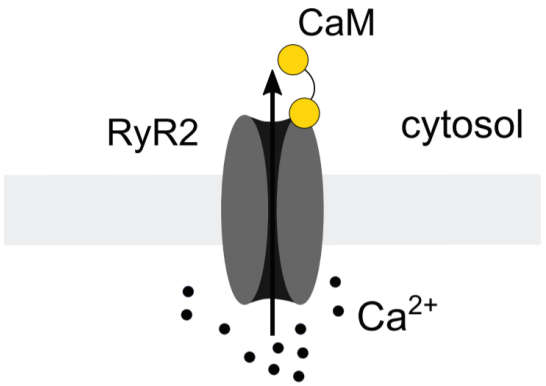


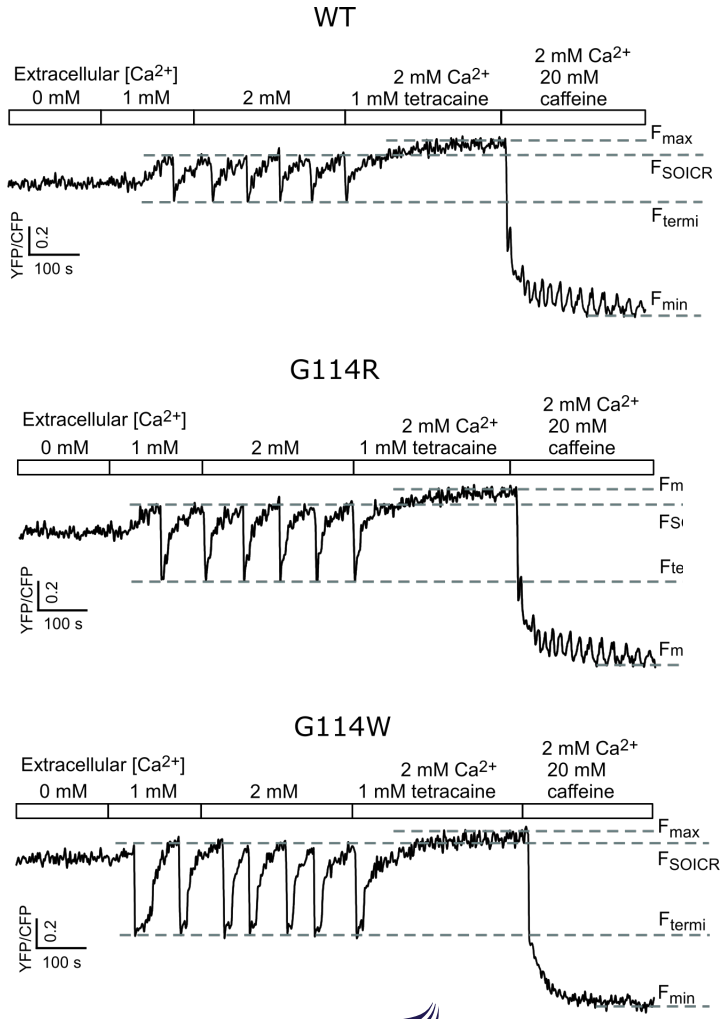


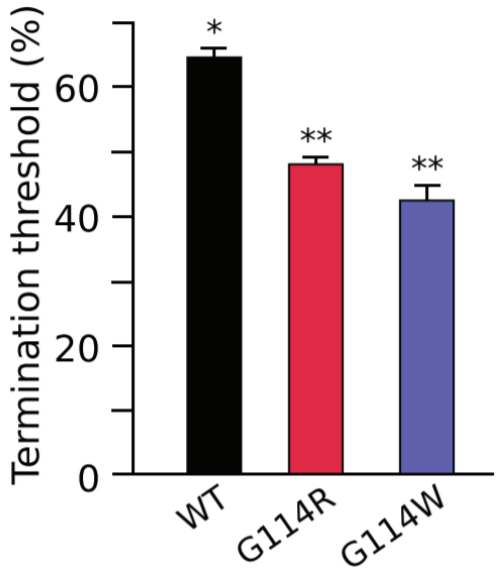


Wayne Chen
(Canada)

Folbigg mutationen forringer calmodulins evne til at lukke RyR2







Wayne Chen
(Canada)

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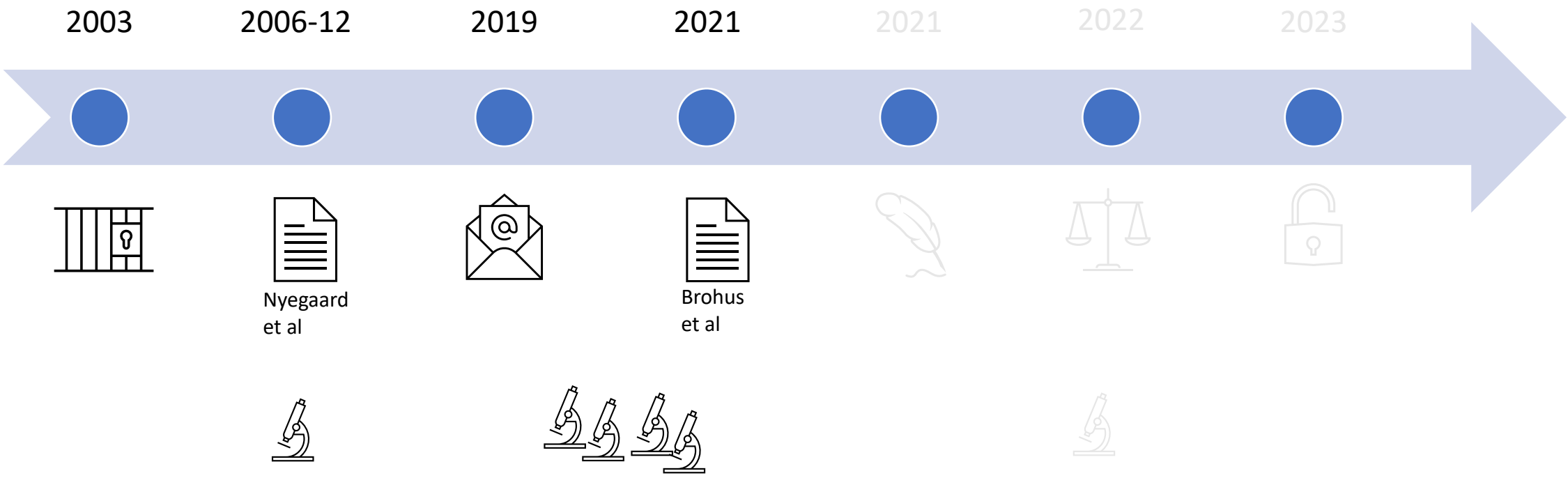
ESC European Society of Cardiology
Europace (2021) 23, 441–450
doi:10.1093/europace/euaa272

CLINICAL RESEARCH
Channelopathies and cardiomyopathies

Infanticide vs. inherited cardiac arrhythmias

Malene Brohus [1†], Todor Arsov[2,3†], David A. Wallace[2†], Helene Halkjær Jensen [1], Mette Nyegaard [4], Lia Crotti [5,6,7], Marcin Adamski[8], Yafei Zhang[9], Matt A. Field [2,10], Vicki Athanasopoulos [2], Isabelle Baró [11], Bárbara B. Ribeiro de Oliveira-Mendes [11], Richard Redon [11], Flavien Charpentier [11], Hariharan Raju [12], Deborah DiSilvestre[13], Jinhong Wei[14], Ruiwu Wang[14], Haloom Rafehi [15,16], Antony Kaspi [15,16], Melanie Bahlo [15,16], Ivy E. Dick [13], Sui Rong Wayne Chen[14], Matthew C. Cook [2], Carola G. Vinuesa [2*‡], Michael Toft Overgaard [1*‡], and Peter J. Schwartz [5*‡]



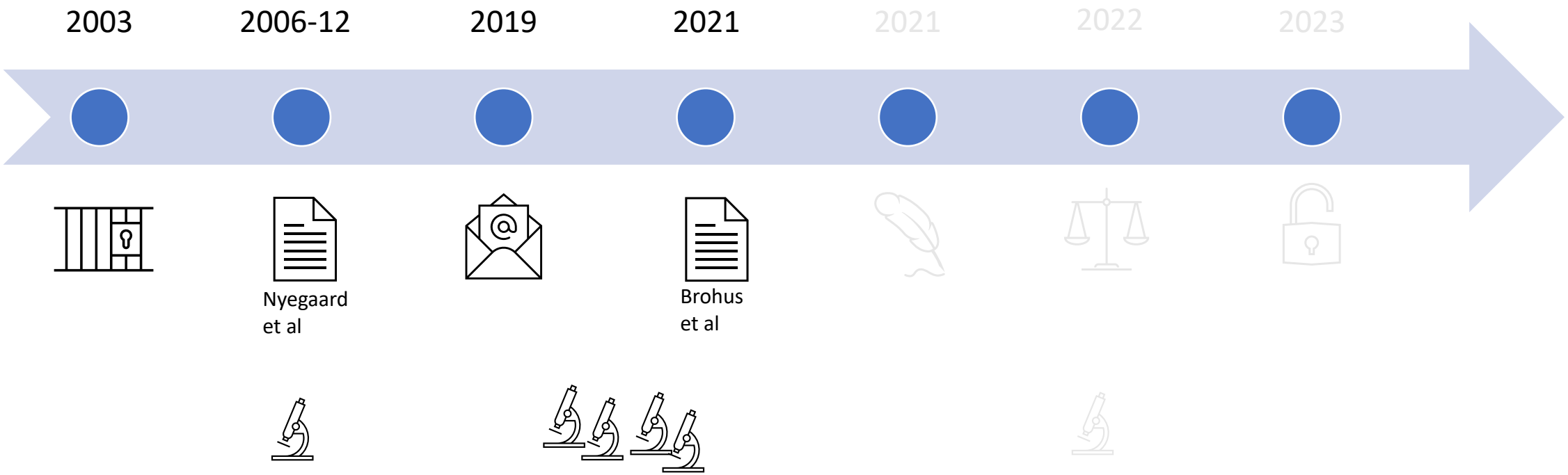
ESC European Society of Cardiology
Europace (2021) 23, 441–450
doi:10.1093/europace/euaa272

CLINICAL RESEARCH
Channelopathies and cardiomyopathies

Infanticide vs. inherited cardiac arrhythmias

Malene Brohus [1†], Todor Arsov[2,3†], David A. Wallace[2†], Helene Halkjær Jensen [1],

Conclusion A novel functional calmodulin variant (G114R) predicted to cause idiopathic ventricular fibrillation, catecholaminergic polymorphic ventricular tachycardia, or mild long QT syndrome was present in two children. A fatal arrhythmic event may have been triggered by their intercurrent infections. Thus, calmodulinopathy emerges as a reasonable explanation for a natural cause of their deaths.



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CLINICAL RESEARCH
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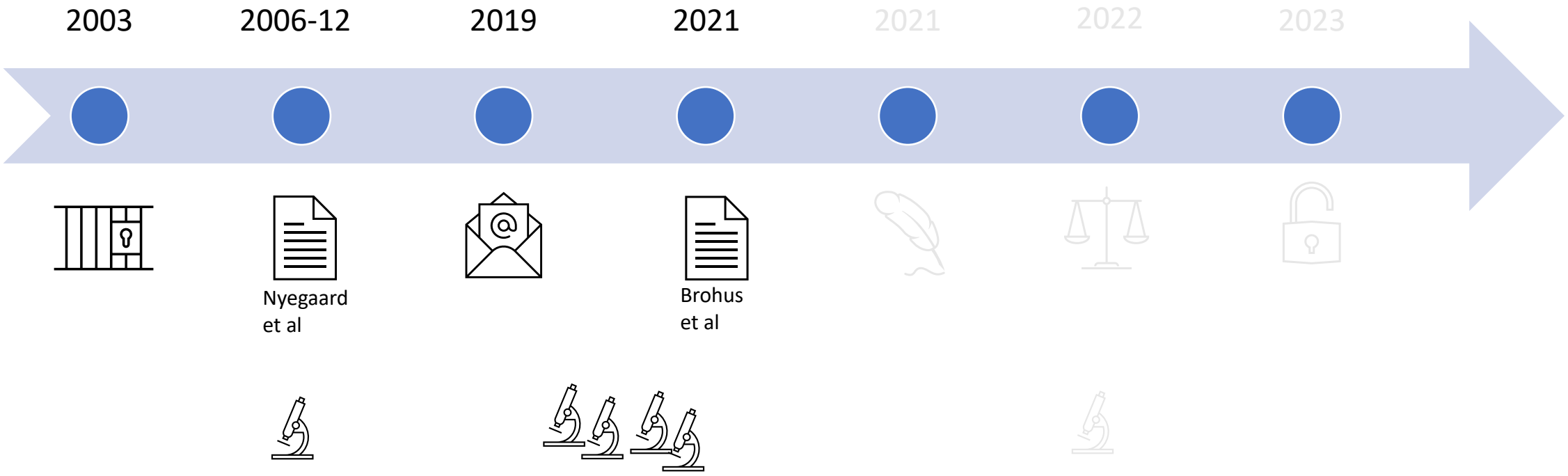
Conclusion A … lation, catecholaminer- … gic … dren. A fatal arrhythmic … eve … nerges as a reasonable … exp …

Det er sandsynligt at calmodulin mutationen G114R har slået Folbigg døtrene ihjel.



6 November, 2022

Bekymringer der nævnes i andre ekspert rapporter:

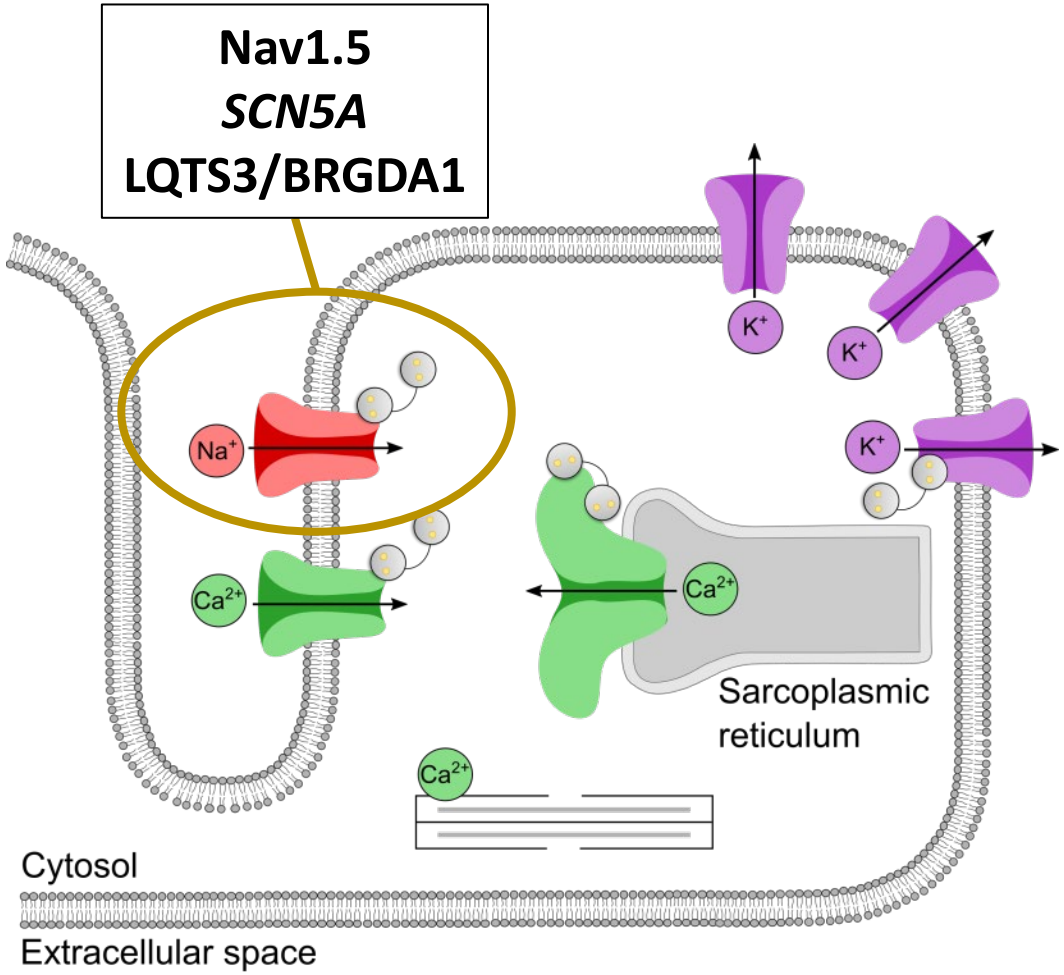
”Sygdomsbilledet i Folbigg familien passer ikke med det sygdomsbillede vi kender fra andre calmodulin-sygdomsforløb”

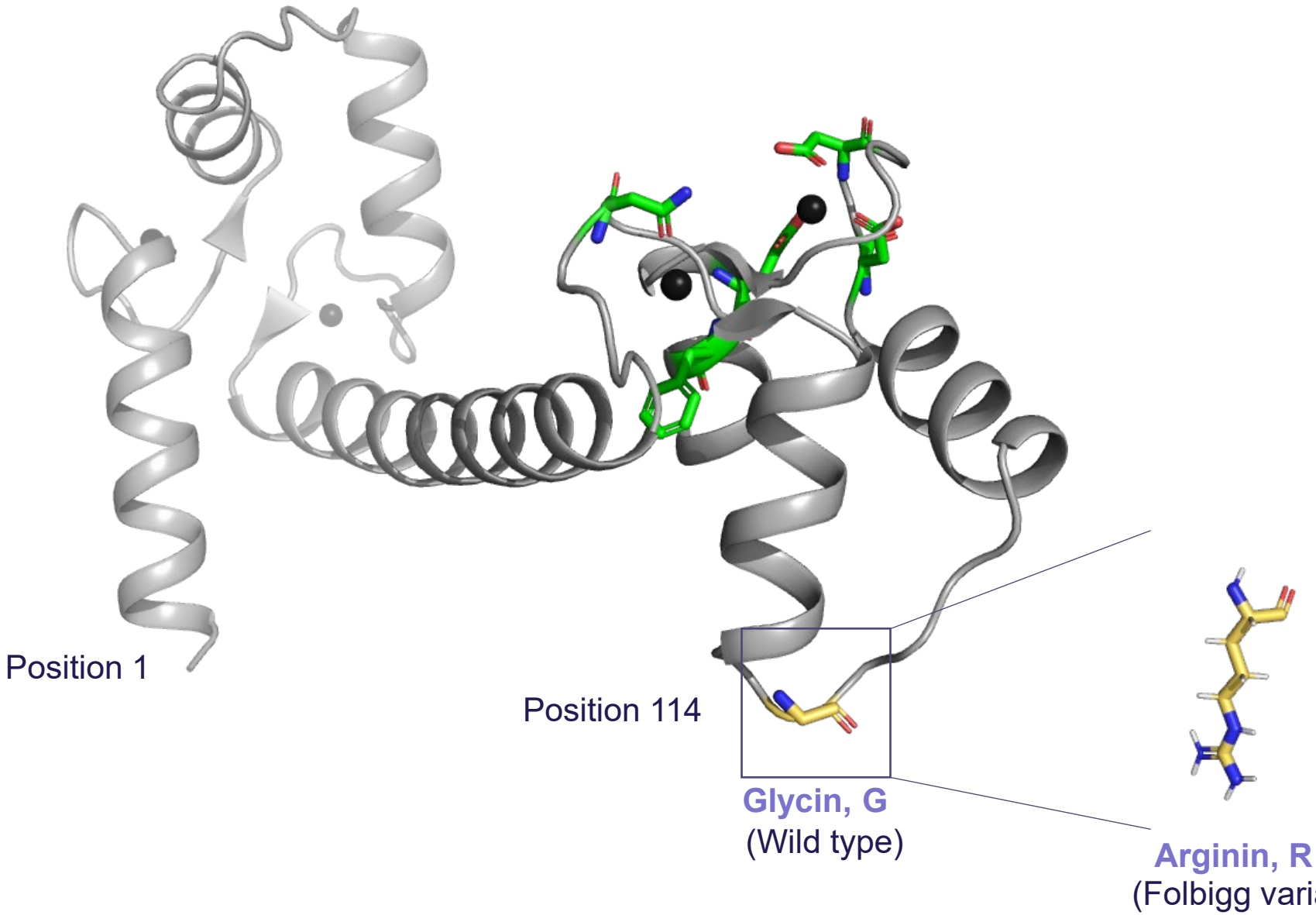
”Feber udløser kun hjertearytmi-anfald i Brugada Syndrome

– en Natrium-kanal sygdom i børn”

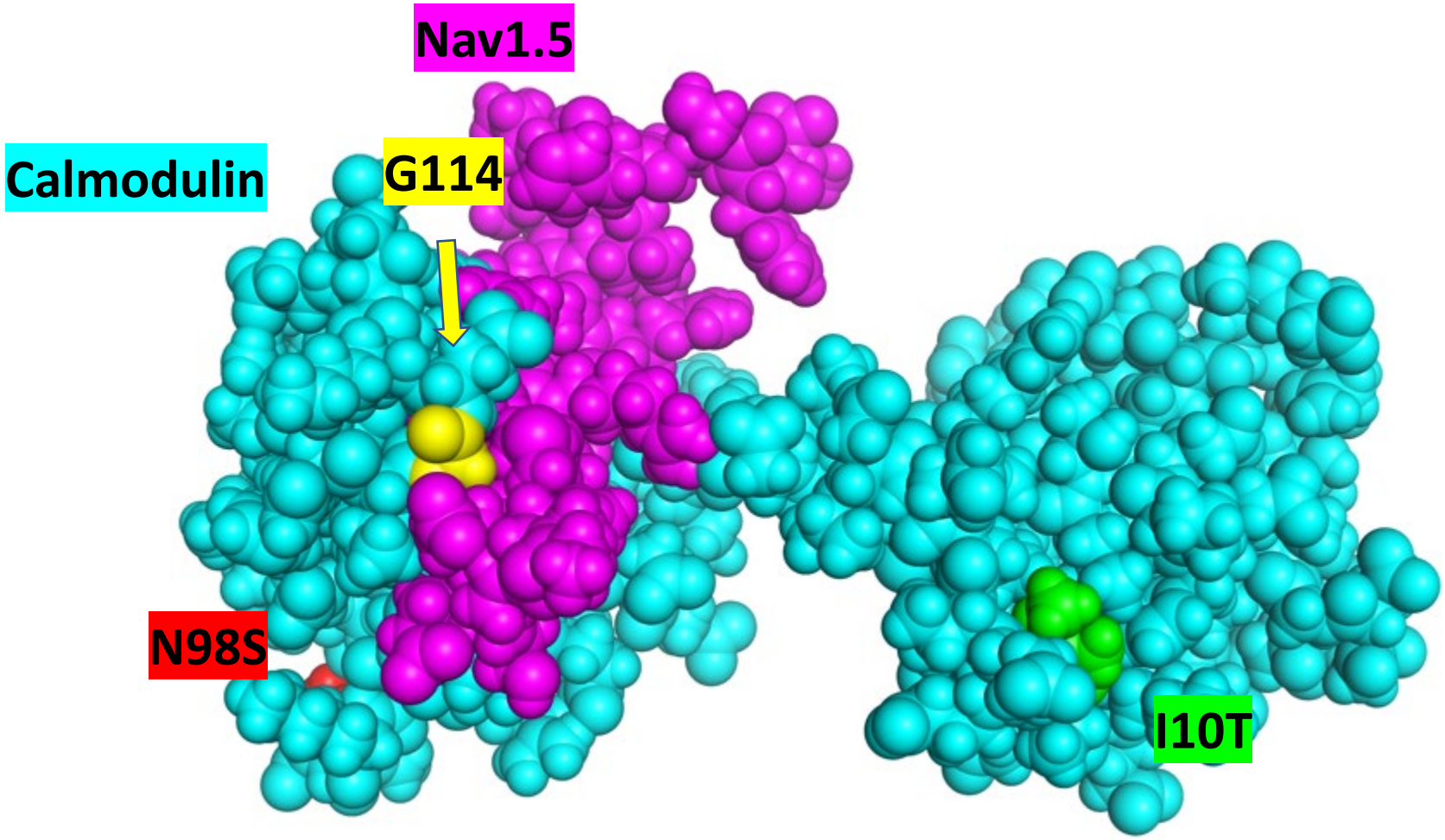
”Kun Natrium-kanal mutationer giver årsag til ‘død mens man sover’! ”

Calmodulin regulerer Nav1.5 – Hjertets Natrium-channel




Position 1
Position 114
Glycin, G
(Wild type)
Arginin, R
(Folbigg variant)

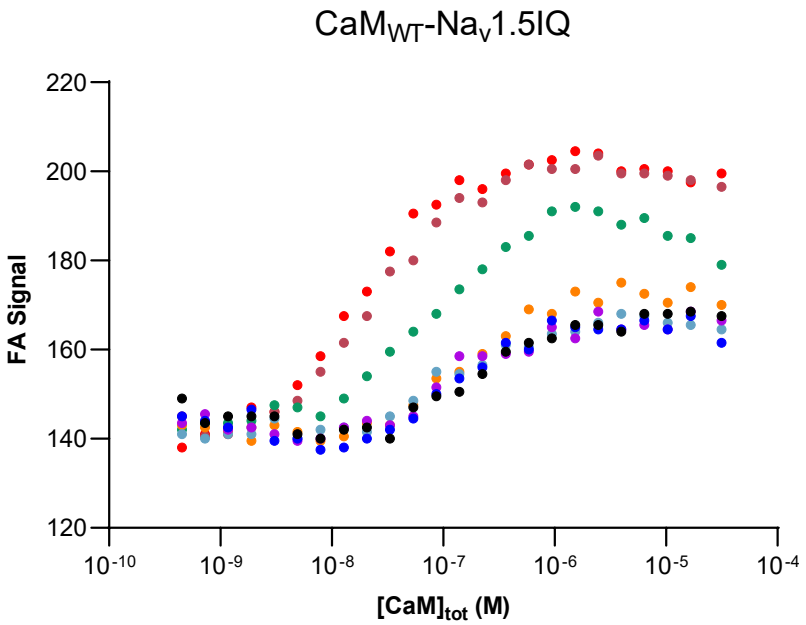
Calmodulin binder til Nav1.5 (peptide)

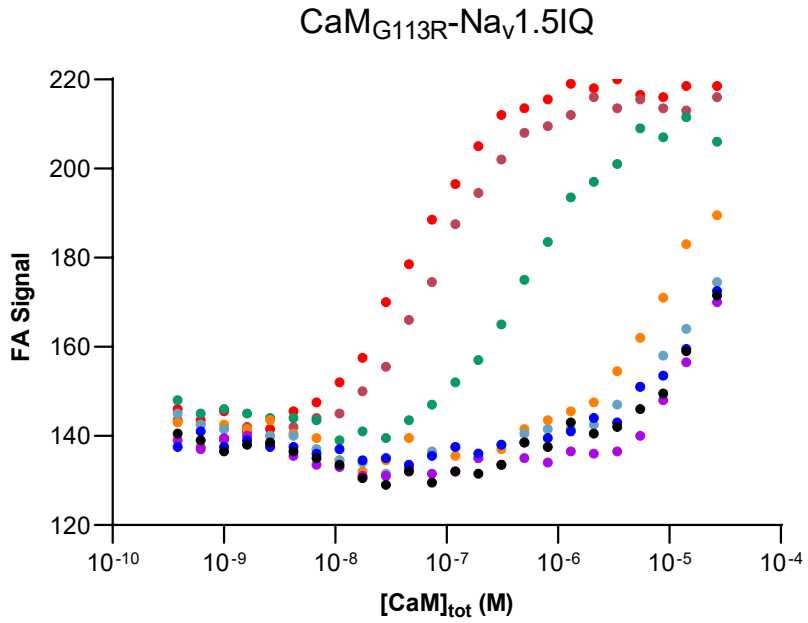


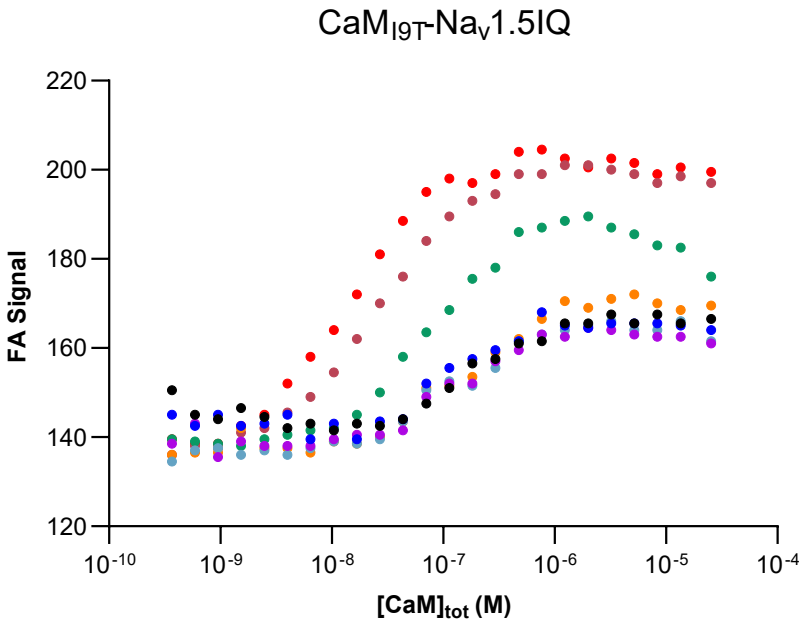
8 November

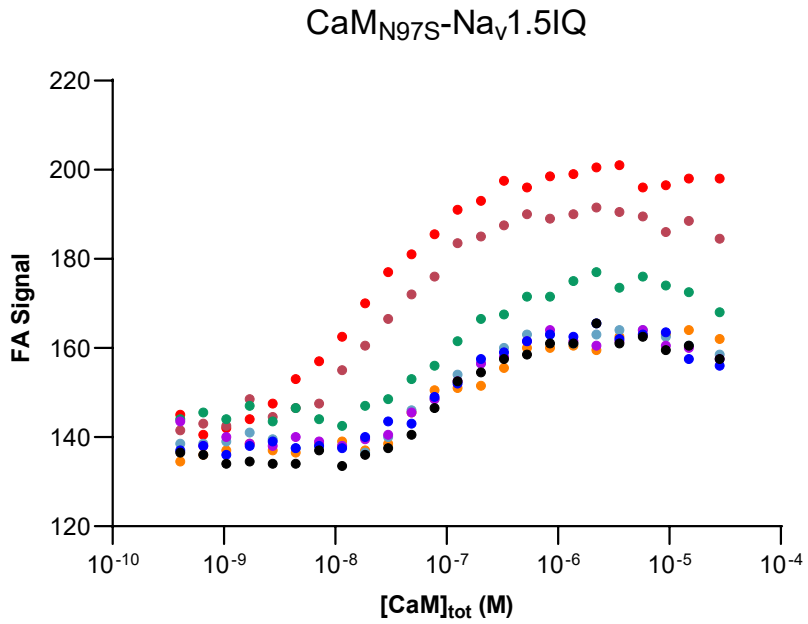
Første dataset!

Ana-Octavia Busuioc, VA



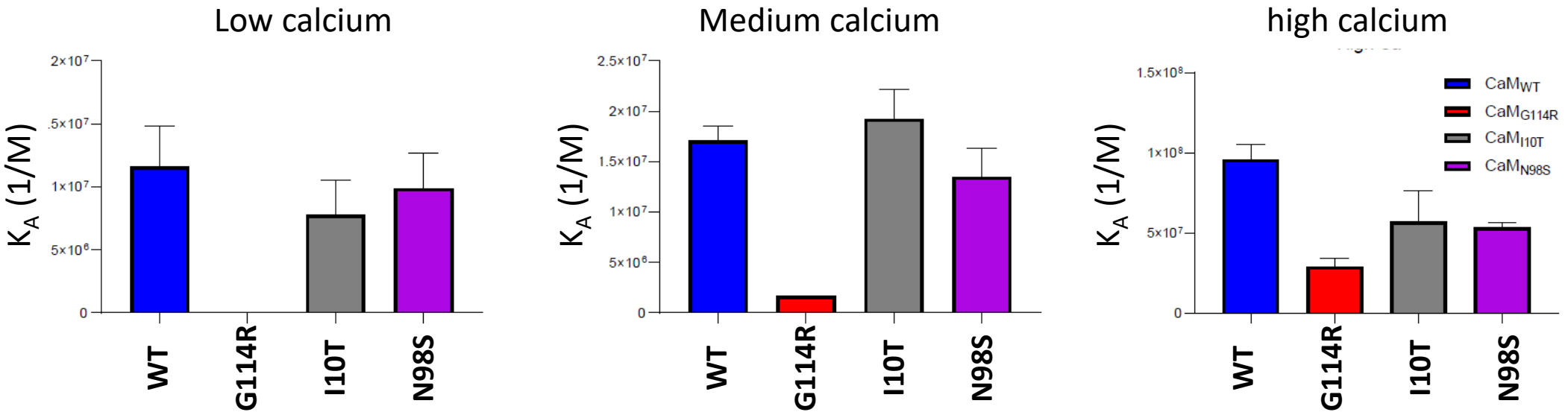






10 November, 6.02am – Zoom Møde

Calmodulin binding to the SCN5A (Nav1.5) IQ-domain



The binding of G114R to the Nav1.5 IQ domain is severely reduced, in particular at low and medium calcium concentrations


RØDE


He's proving very popular, showing his authentic side and has plugged into the mood of the nation
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WHY FOLBIGG INQUIRY HAD TO BE ADJOURNED
Explosive new evidence has seen a three-month postponement. Jane Hansen explains why

ABC NEWS

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For local weather

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Kathleen Folbigg inquiry examines new scientific evidence and 'likely genetic mutation'

By court reporter Jamelle Wells

Posted Tue 15 Nov 2022 at 6:11am, updated Wed 16 Nov 2022 at 12:31am

Professor Nyegaard (left), and Professor Overgaard say the mutation was "unlucky" for families. *(AAP:*

COSMOS

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Folbigg Inquiry: Mutations in calmodulin were considered "incompatible with life" until a breakthrough discovery

Professors Michael Toft Overgaard and Mette Nyegaard / Source: Aalborg University

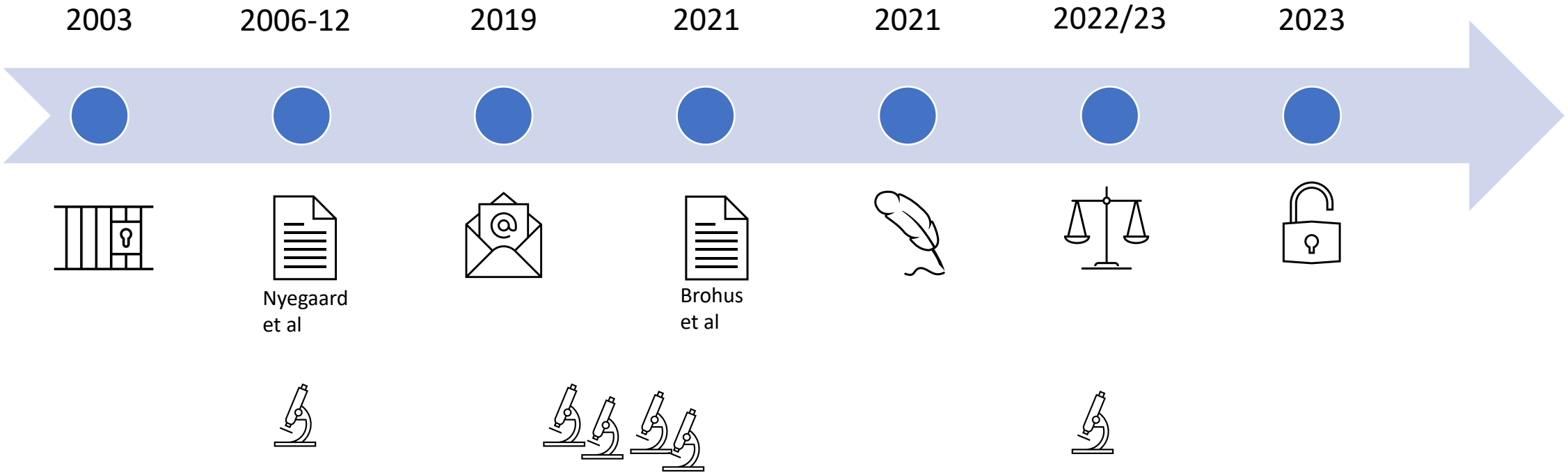
15 November 2022

Matthew Ward Agius

The inquiry into the convictions of Kathleen Folbigg has heard that, until discovered in 2012, mutations to the genes that produce the important regulatory protein calmodulin were considered incompatible with life.

Husband-and-wife professors Michael Toft Overgaard and Mette Nyegaard, from Aalborg University in Denmark, were the sole experts to present evidence to the inquiry in Sydney today. Due to their presentation of what Tom Bathurst KC, conducting the inquiry, described as "new and quite exceptional" information, they are the final witnesses in this hearing

Juni 2023


2003
2006-12
2019
2021
2021
2022/23
2023
Nyegaard et al
Brohus et al


NEWS FIRST
KATHLEEN FOLBIGG PARDONED


BREAKING NEW
KATHLEEN FOLBIGG 'PARDONED'
RECOMMENDATIONS MADE AFTER AN INQUIRY


FOLBIGG REUNITES WITH LOVED ONES AFTER PARDON
EXCLUSIVE
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9 NEWS
WATCH LIVE 6PM

nature

NEWS | 06 June 2023

‘Science was heard’: woman who was convicted of killing her children pardoned after inquiry

Kathleen Folbigg, who was jailed in Australia in 2003 over the sudden deaths of her four young children, has been pardoned and released in the wake of new scientific evidence.

Dyani Lewis

Læs og hør mere om sagen

LUNDBECKFONDEN

”Danish research could lead to acquittal of Australian woman for the deaths of her four children - she has served 18 years in prison”
Artikel-serie
13. marts 2021

Jyllands-Posten

”Danske forskere fandt genbevis, der kan føre til benådning af den mest forhadte kvinde i Australien”
Tema-artikler
27. marts 2021

”Gen som bevis”
Podcast, DR
31. marts 2021

”Genstart: mor og morder?”
Podcast, DR
14. april 2021

Videnskab dk

”Dansk forskning kan frikende kvinde, der er fængslet for drab på sine børn”
Artikel-serie
December 2021

Læs mere om sagen

The New York Times

She Was Imprisoned for Killing Her 4 Children. But Was It Their Genes All Along?

The case of Kathleen Folbigg has become a contest between cutting-edge science and an Australian court system that sometimes ignores it.

abc NEWS

Australian mom convicted of killing 4 children seeks pardon

Nearly two decades after an Australian woman was convicted of killing her four children, dozens of scientists are backing the claim that they may have died of natural causes

The Washington Post
Democracy Dies in Darkness

World

An Australian mom was convicted of killing her 4 babies. Scientists say she's innocent.

BBC

Kathleen Folbigg: Could science free Australian jailed for killing babies?

CNN

Genetics may free a woman convicted of killing her 4 babies and help other parents explain the unexplainable


Spørgsmål?