



dravet CANADA

# DRAVET DAY MONTREAL

14 AVRIL 2018 - APRIL 14 2018

CHU SAINT-JUSTINE, MONTREAL, QUEBEC

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# Modéliser le syndrome de Dravet chez le poisson-zèbre

Nouvelles données sur les mécanismes et futures stratégies thérapeutiques personnalisées.

# Modelling Dravet Syndrome in zebrafish

New insights on the mechanisms and future personalized therapeutic strategies

# EPILEPSIES

Absence seizures  
Absence épileptique

Generalized  
Généralisée

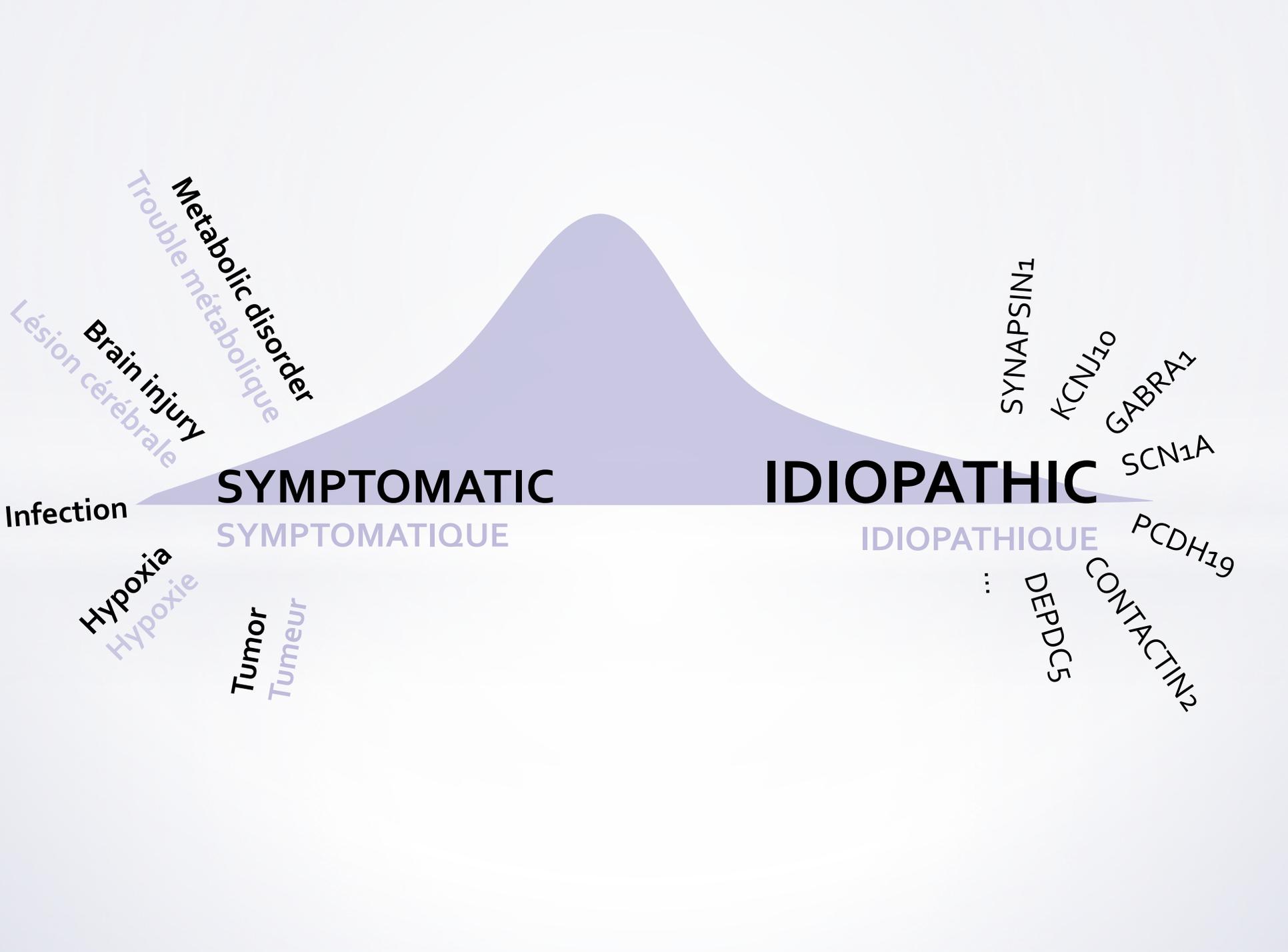
Juvenile myoclonic  
Myoclonique juvénile

Febrile seizures  
Convulsions fébriles

Dravet syndrome  
Syndrome de Dravet

Multiple foci  
Foyers multiples

Secondarily generalized  
Secondairement généralisée



**SYMPTOMATIC**

**IDIOPATHIC**

SYMPTOMATIQUE

IDIOPATHIQUE

Metabolic disorder  
Trouble métabolique

Brain injury  
Lésion cérébrale

Infection

Hypoxia  
Hypoxie

Tumor  
Tumeur

SYNAPSIN1

KCNJ10

GABRA1

SCN1A

...

DEPDC5

PCDH19  
CONTACTIN2

# DRAVET SYNDROME

**GABRA1**

SCN1A

SYNAPSIN1

KCNJ10

GABRA1

SCN1A

PCDH19

CONTACTIN2

EPDC5

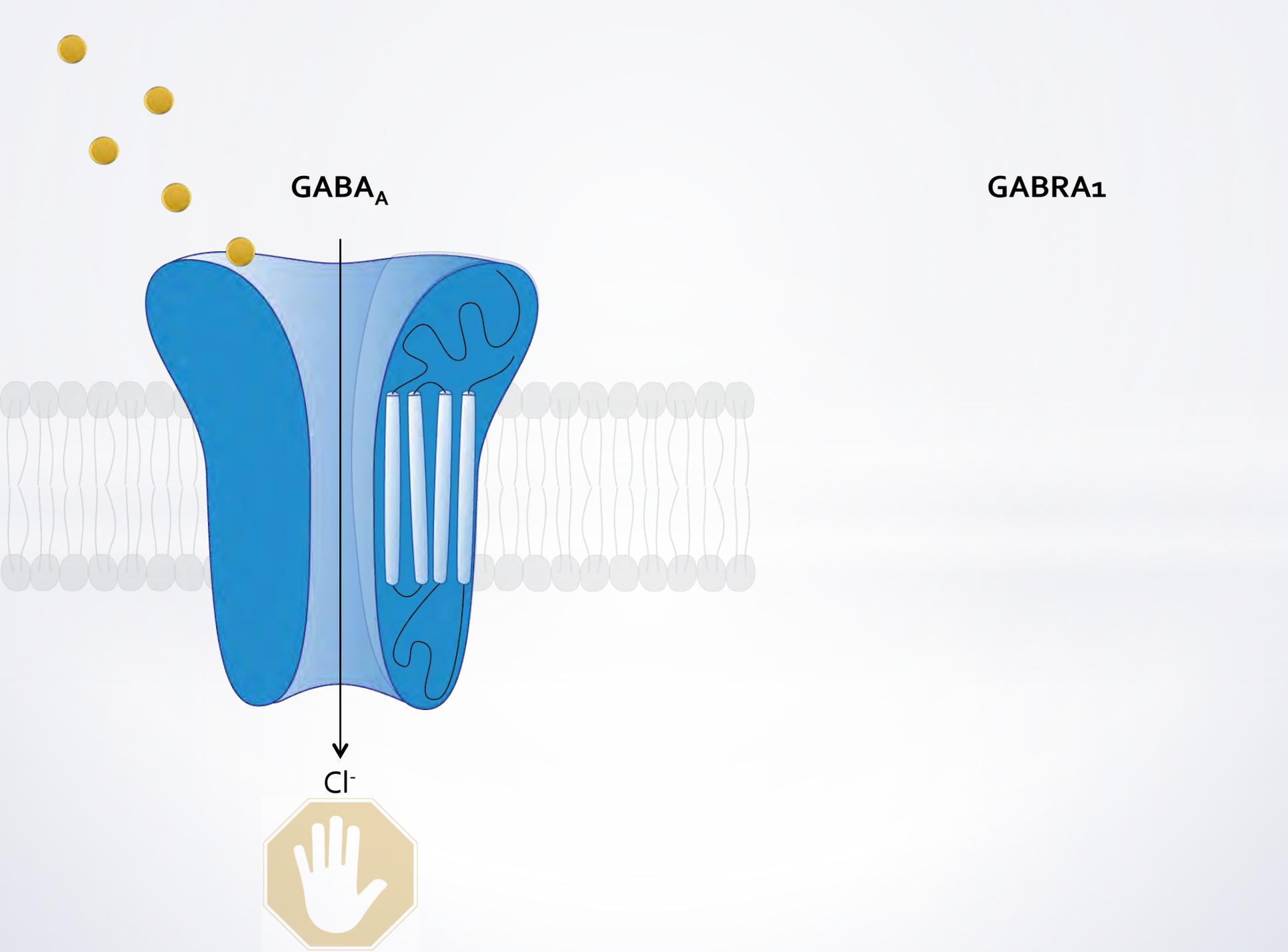
GABRG2

STXBP1

PCDH19

?

DRAVET SYNDROME DE DRAVET



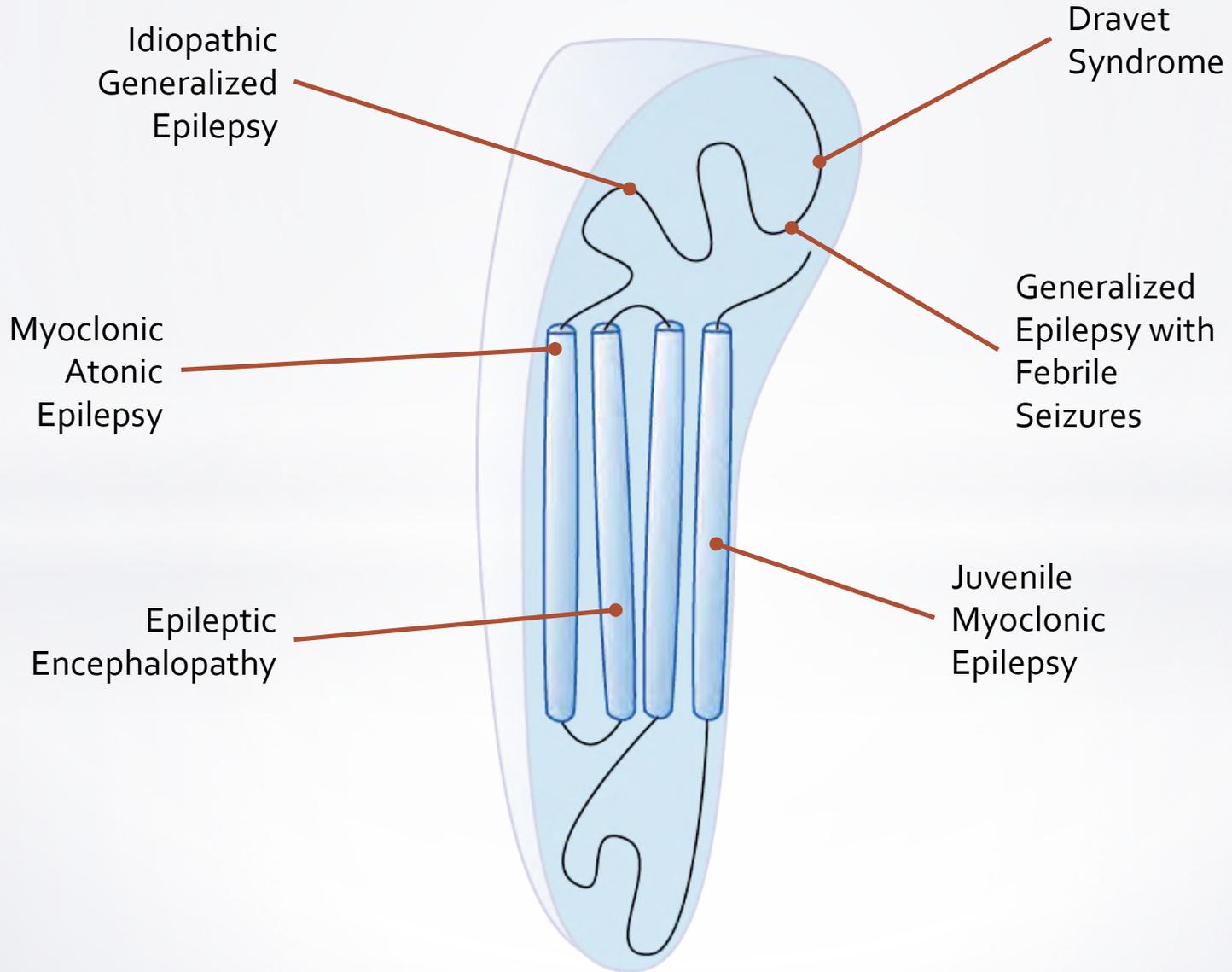
GABA<sub>A</sub>

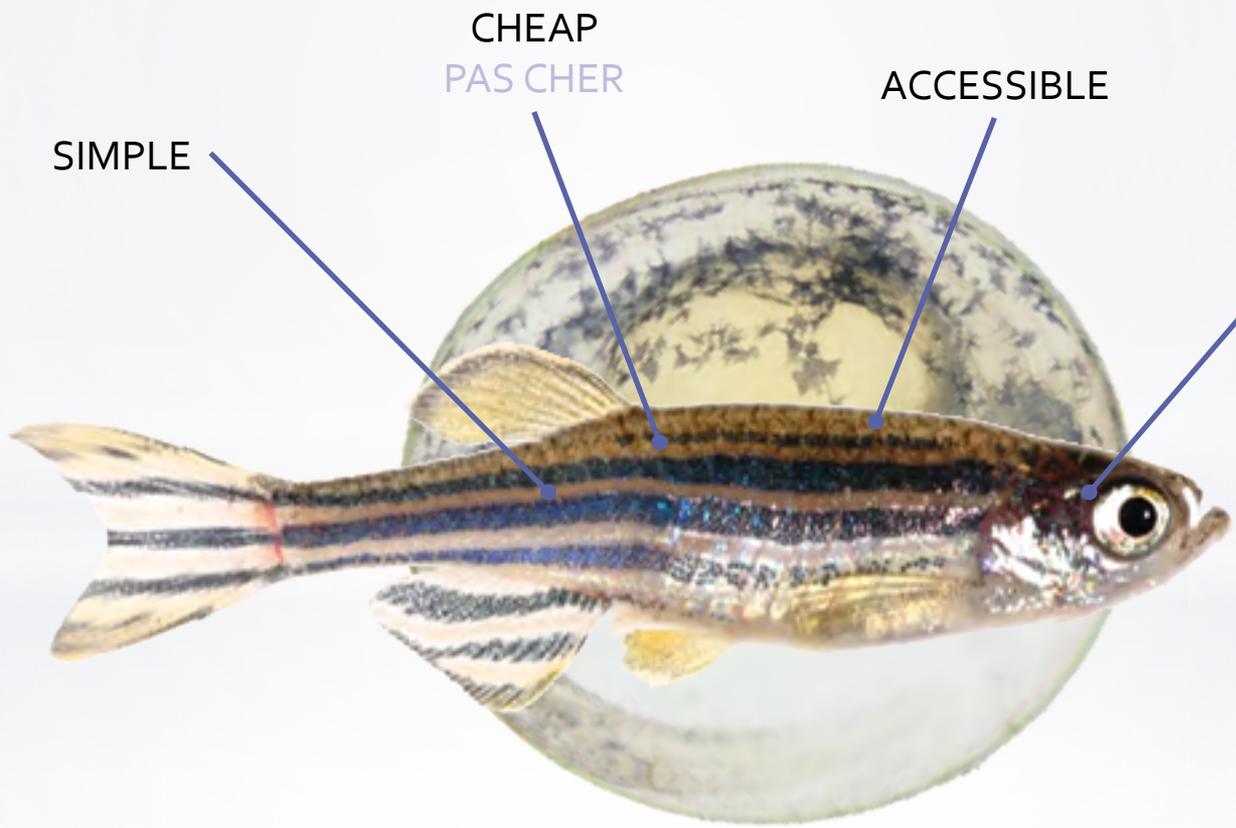
GABRA1

Cl<sup>-</sup>



# GABRA1





SIMPLE

CHEAP  
PAS CHER

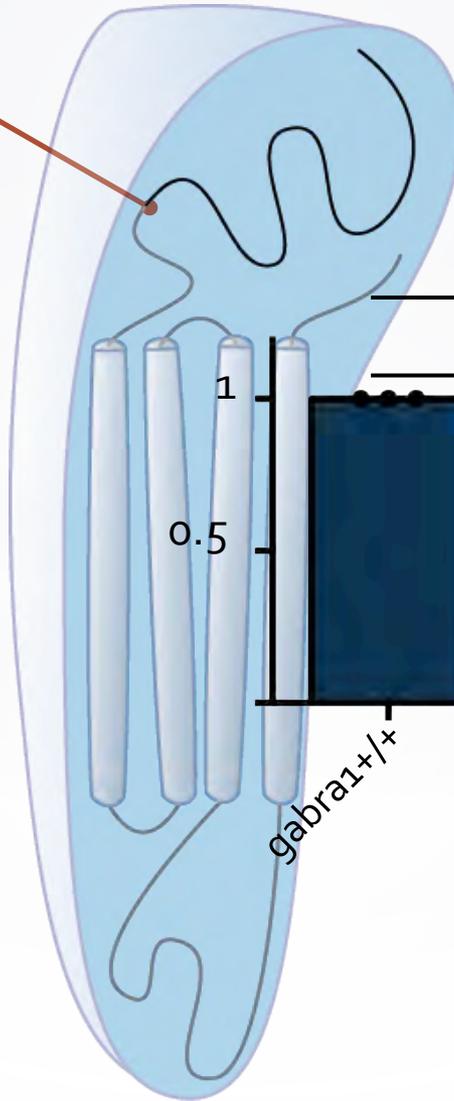
ACCESSIBLE

BRAIN!  
CERVEAU!



# GABRA1<sup>KO</sup>

CRIPSR/CAS9

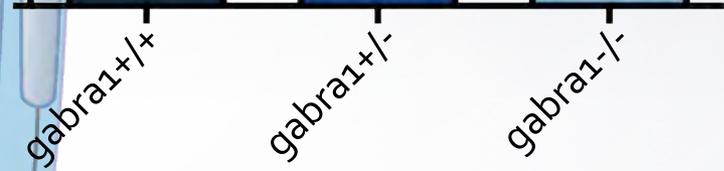


*gabra1* mRNA

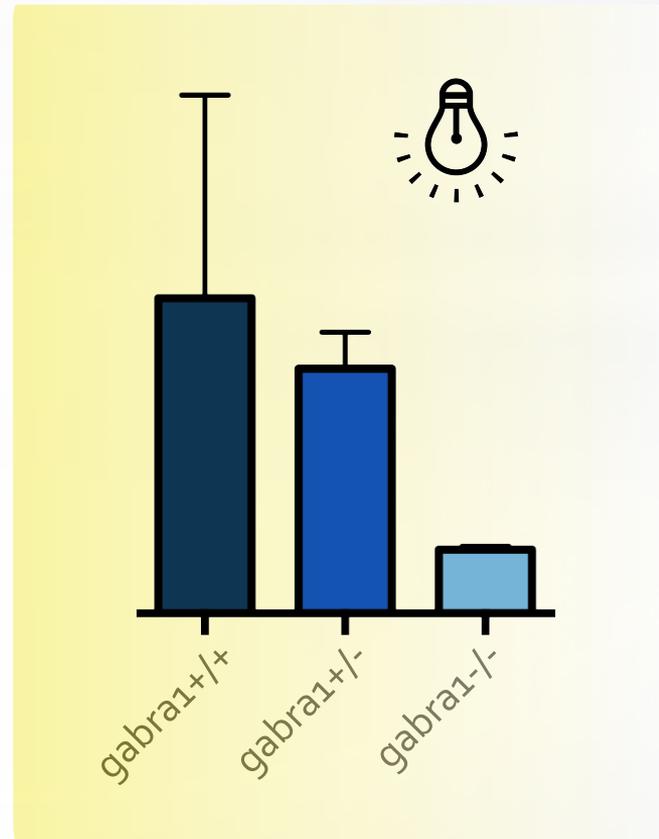
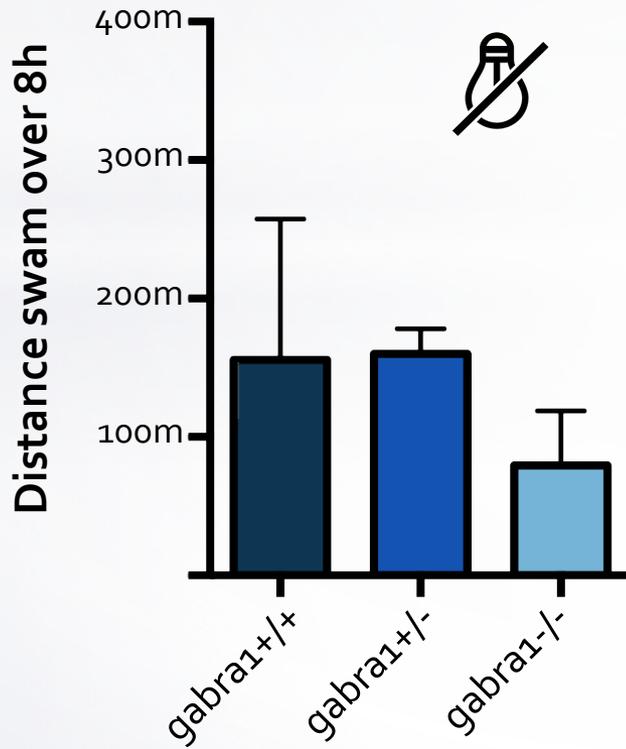
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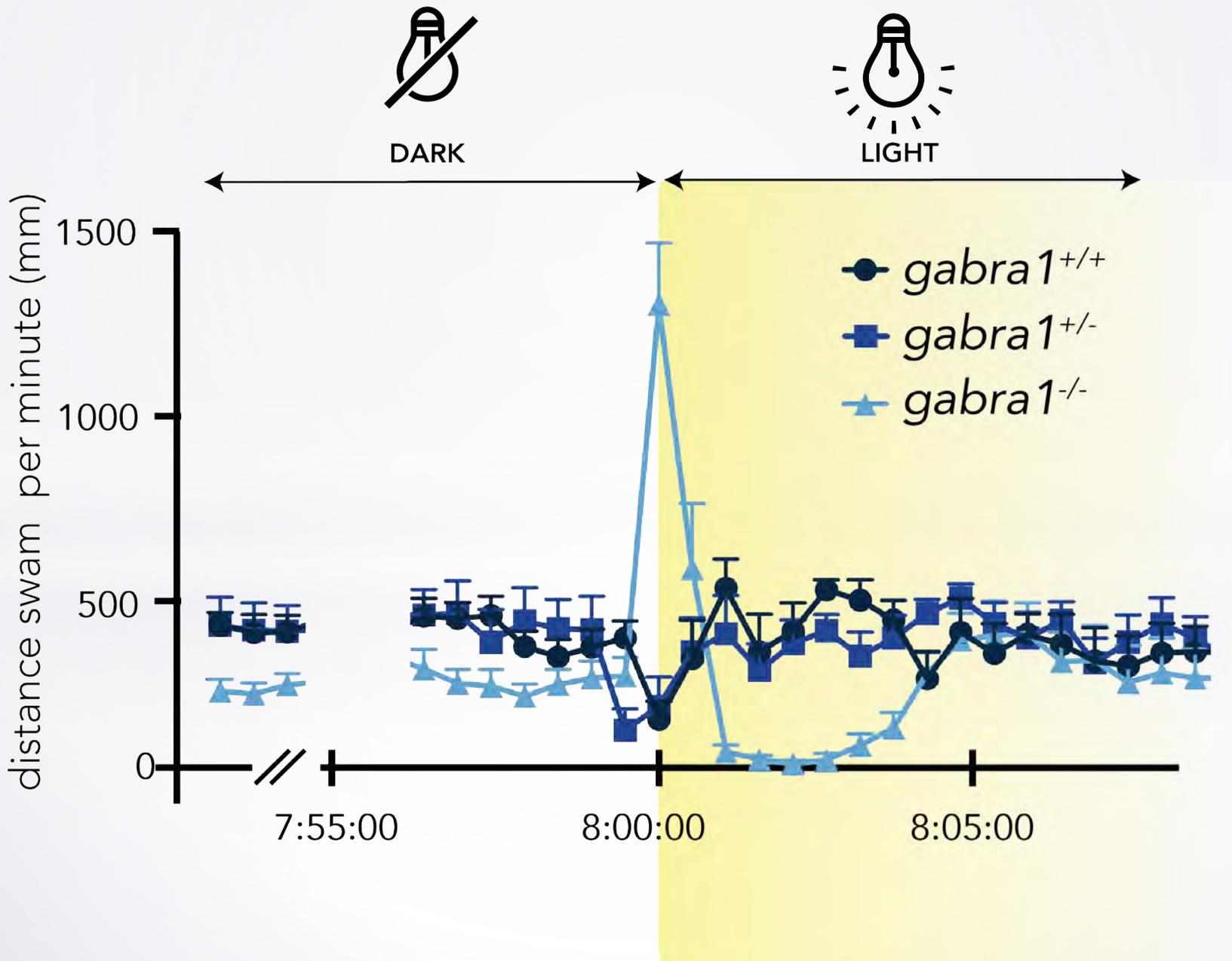
\*\*\*\*

1  
0.5

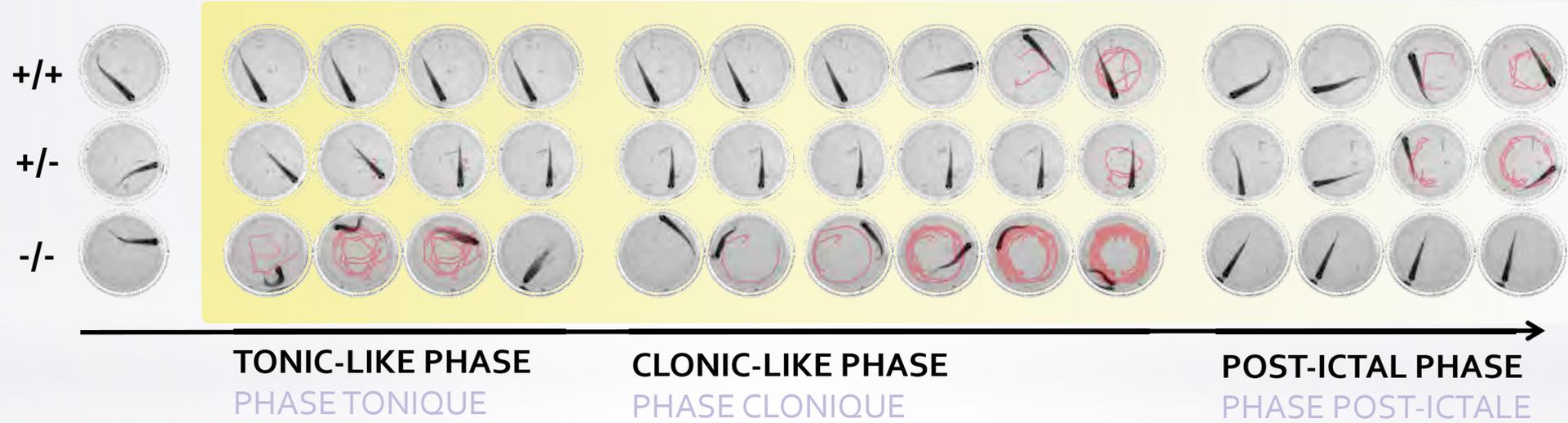


# GABRA1<sup>KO</sup>











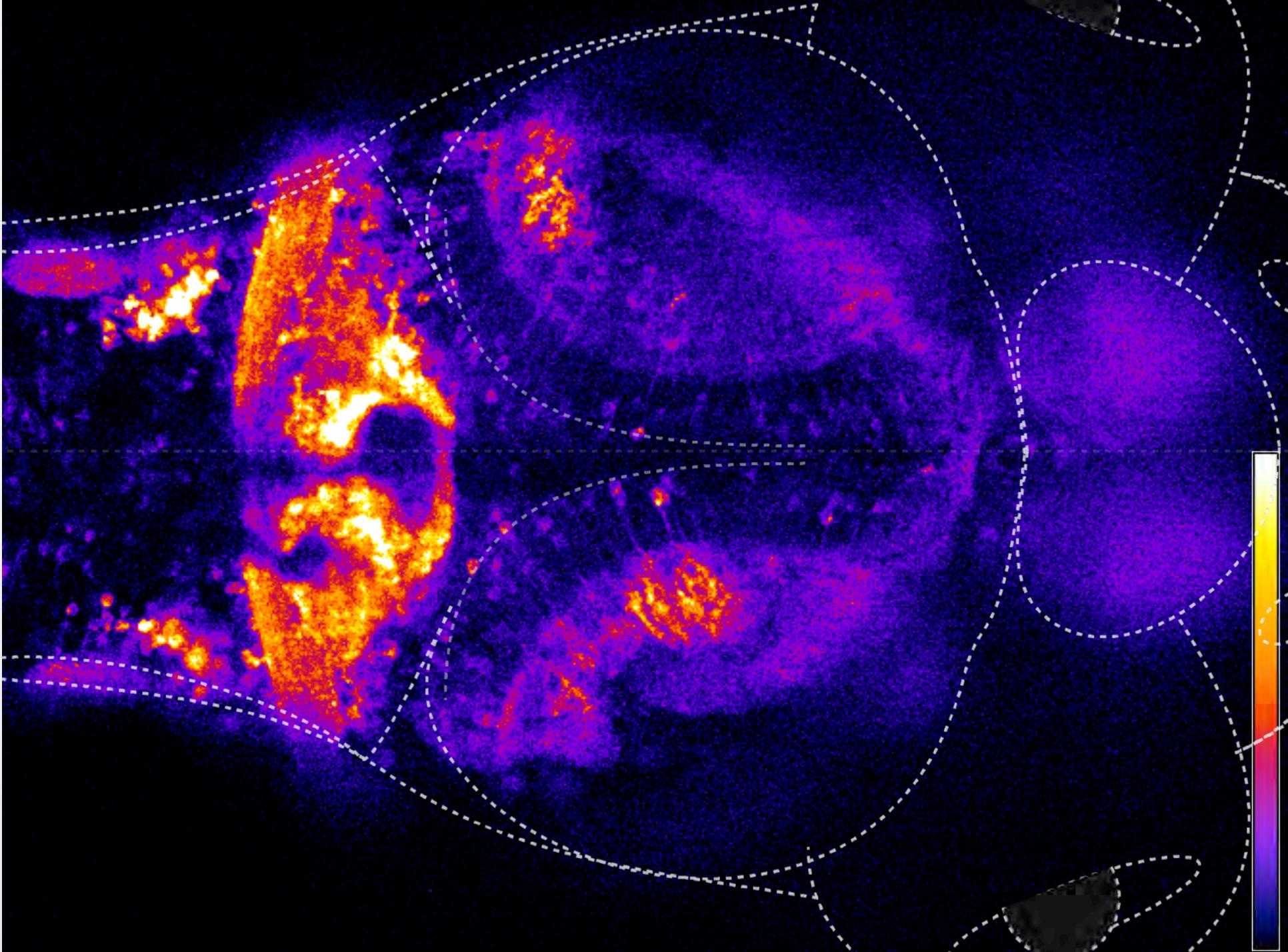
$gabra1^{+/+}$



$gabra1^{+/-}$



$gabra1^{-/-}$

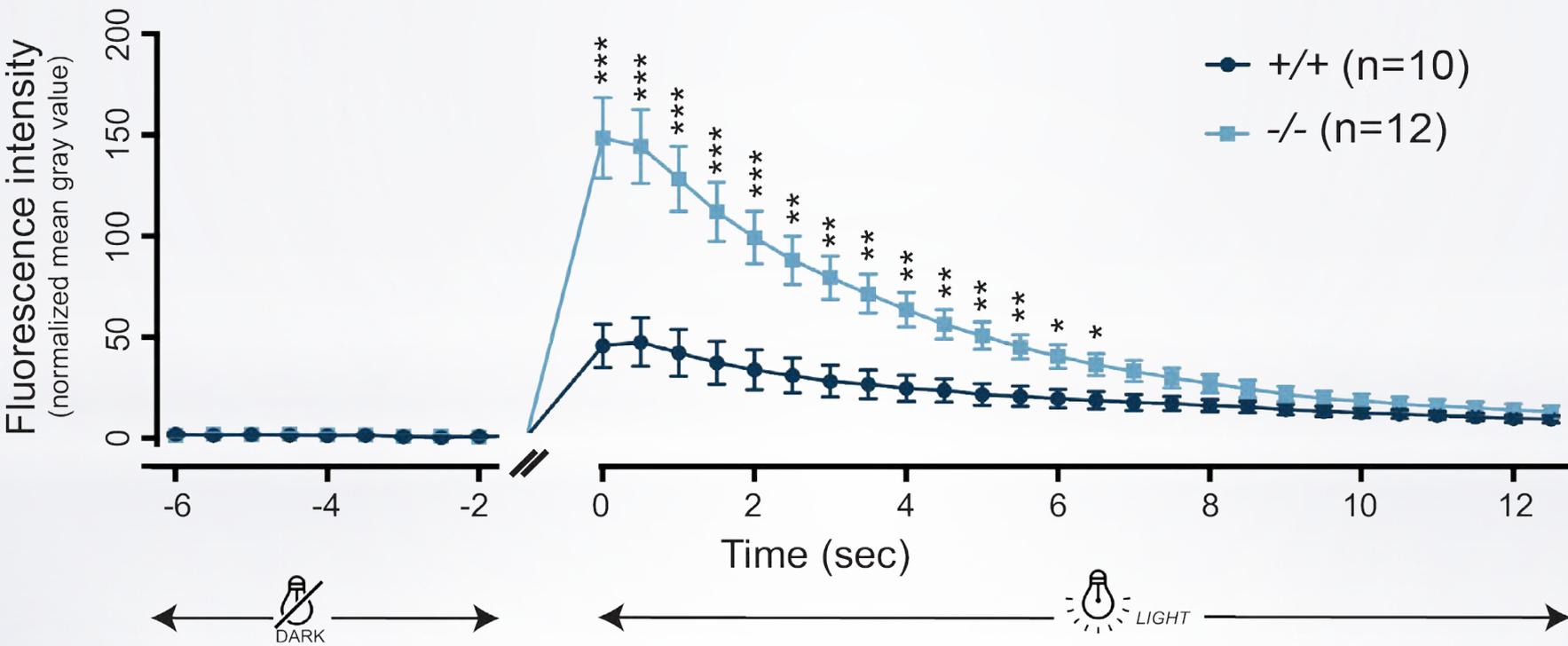




+/+

-/-





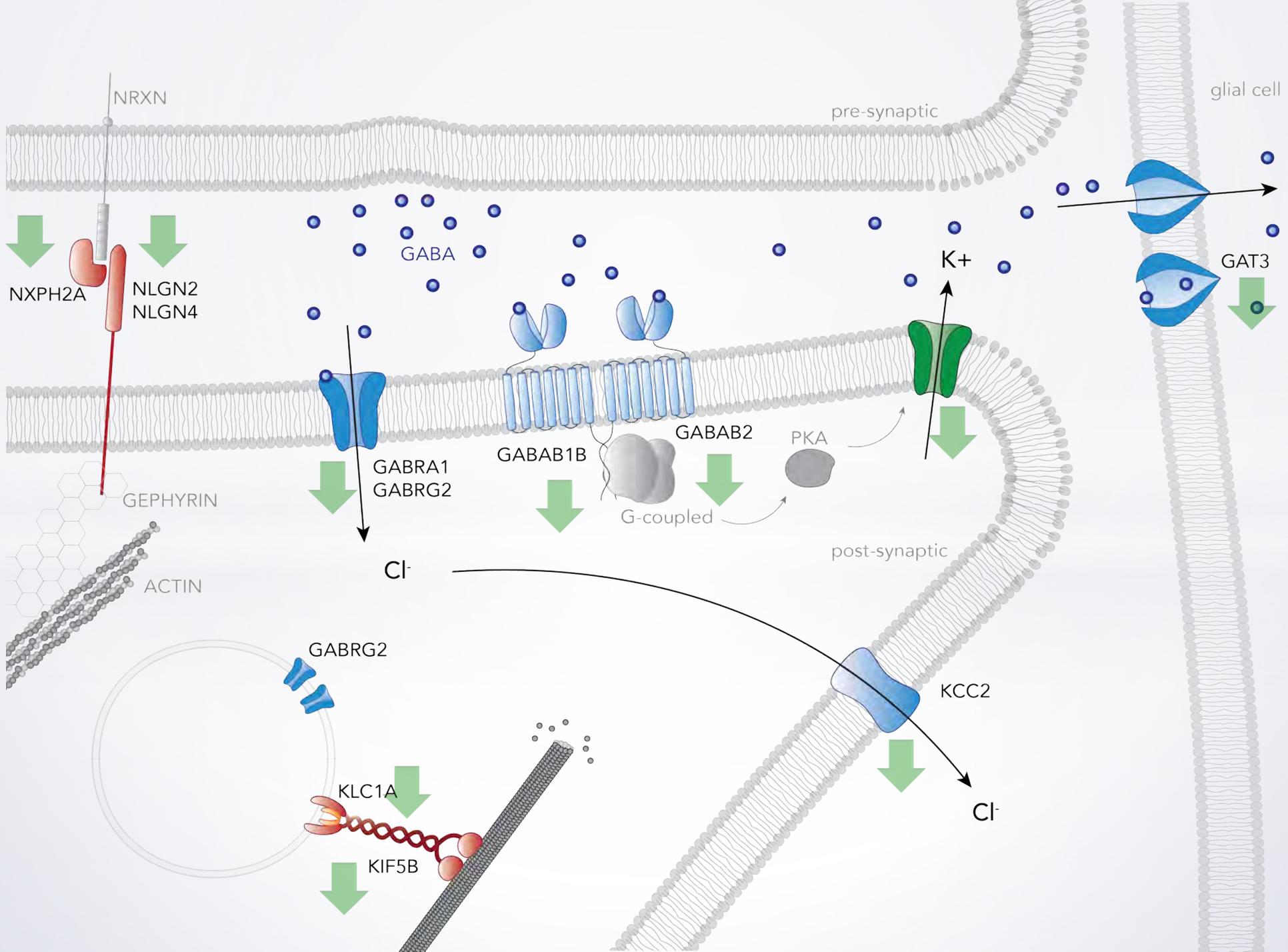






$+/+$  vs  $-/-$

**460 GENES**

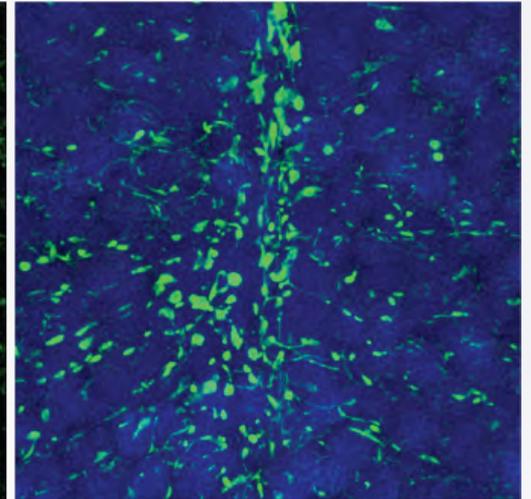
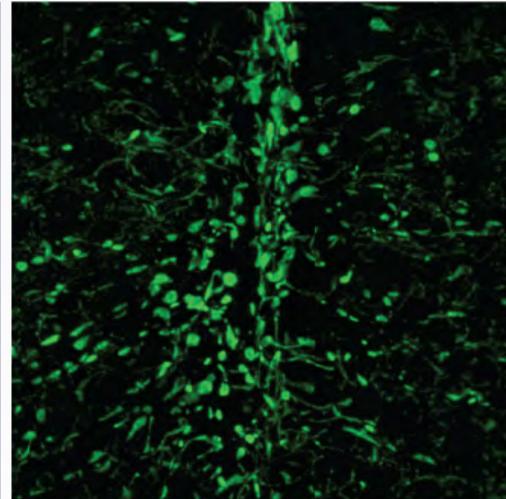
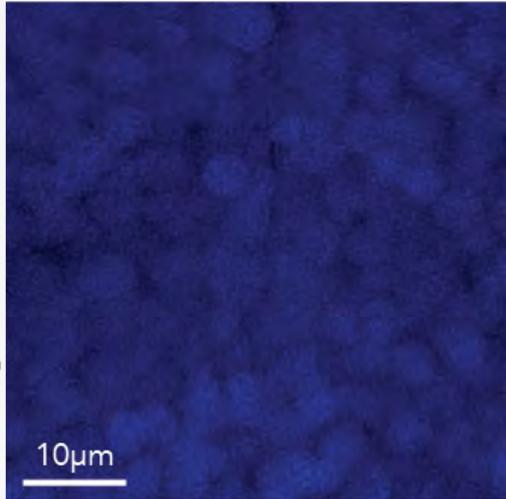


DAPI

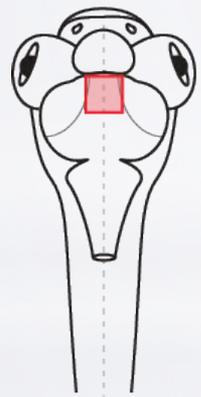
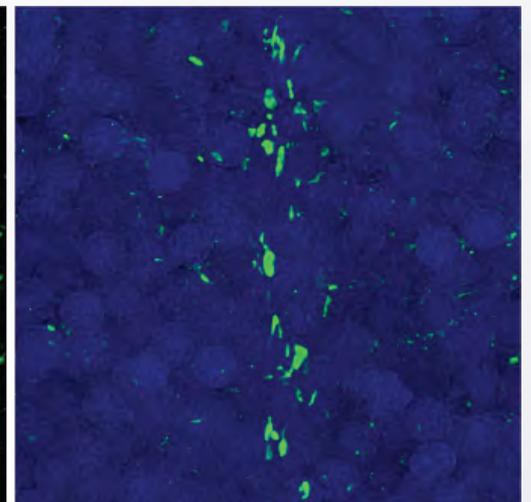
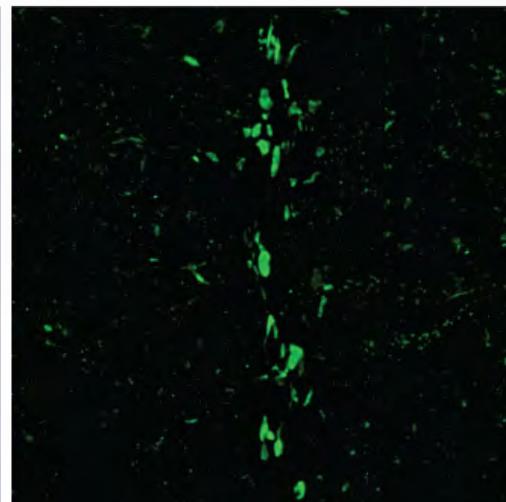
GAD65/67

merge

*gabra1*<sup>+/-+</sup>

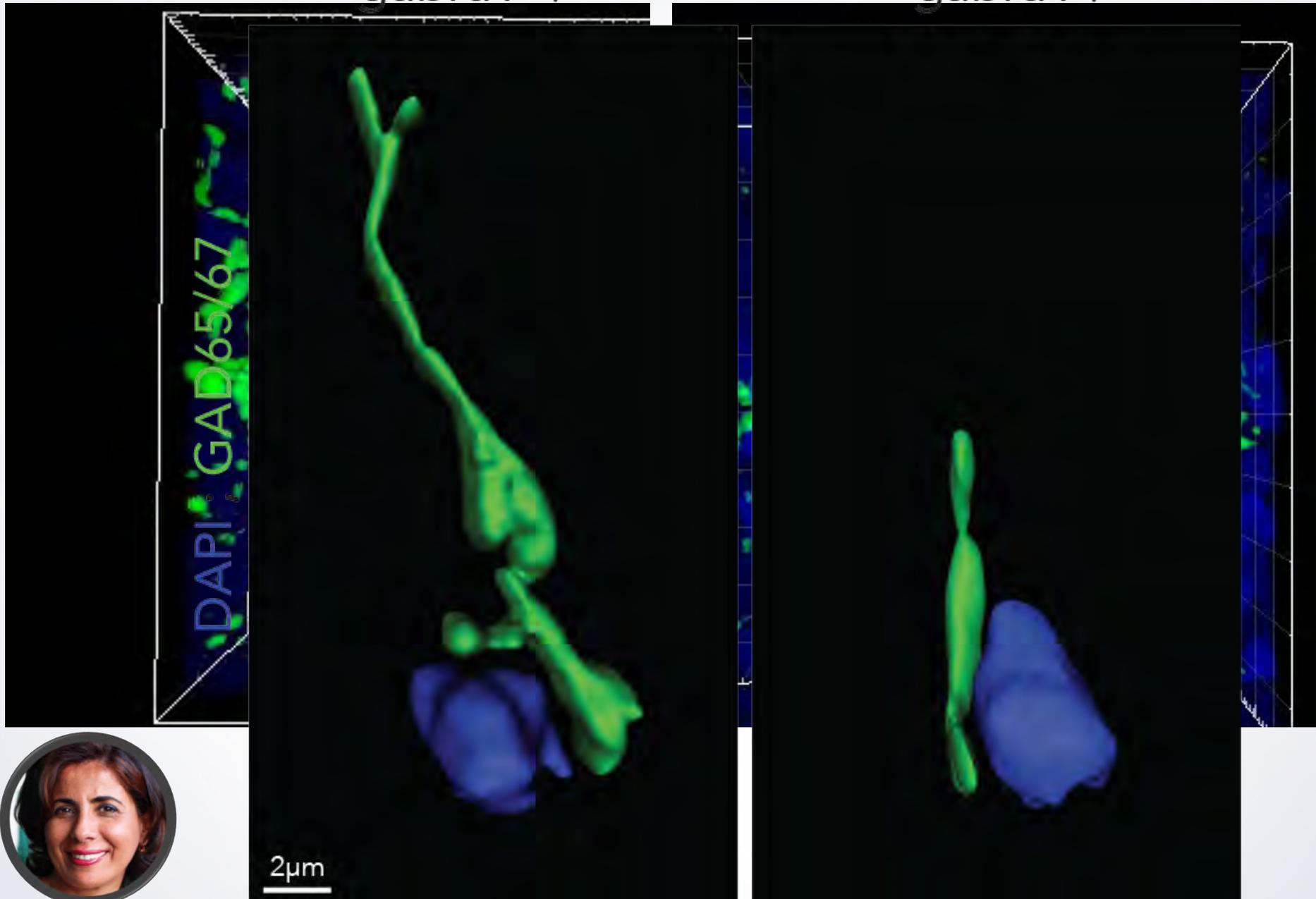


*gabra1*<sup>-/-</sup>

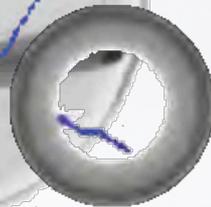
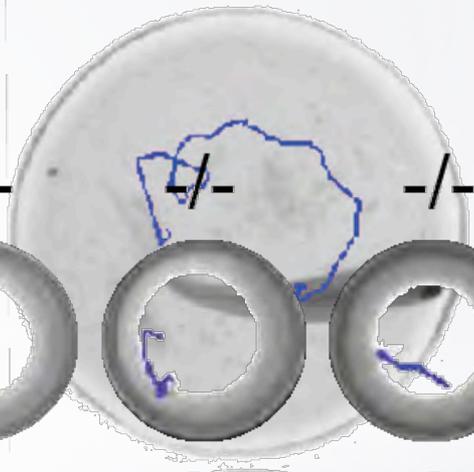
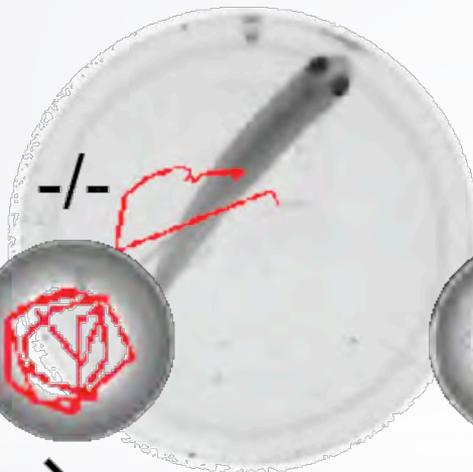
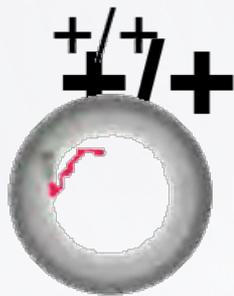


*gabra1* +/+

*gabra1* -/-







untreated

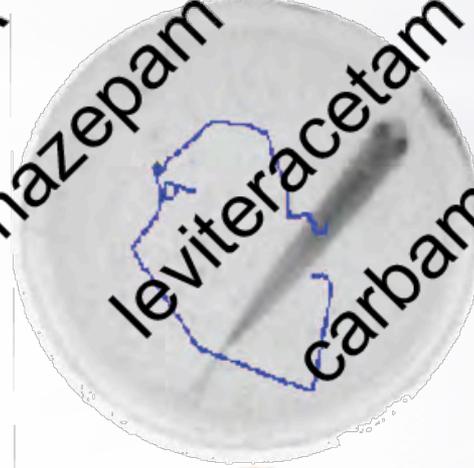
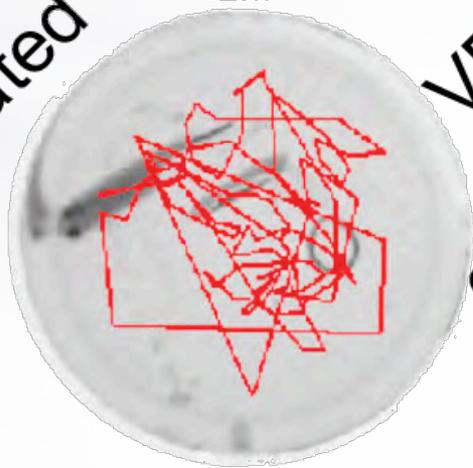
untreated

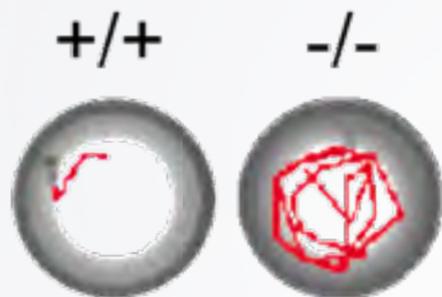
VPA

clonazepam

leviteracetam

carbamazepine





untreated



THC



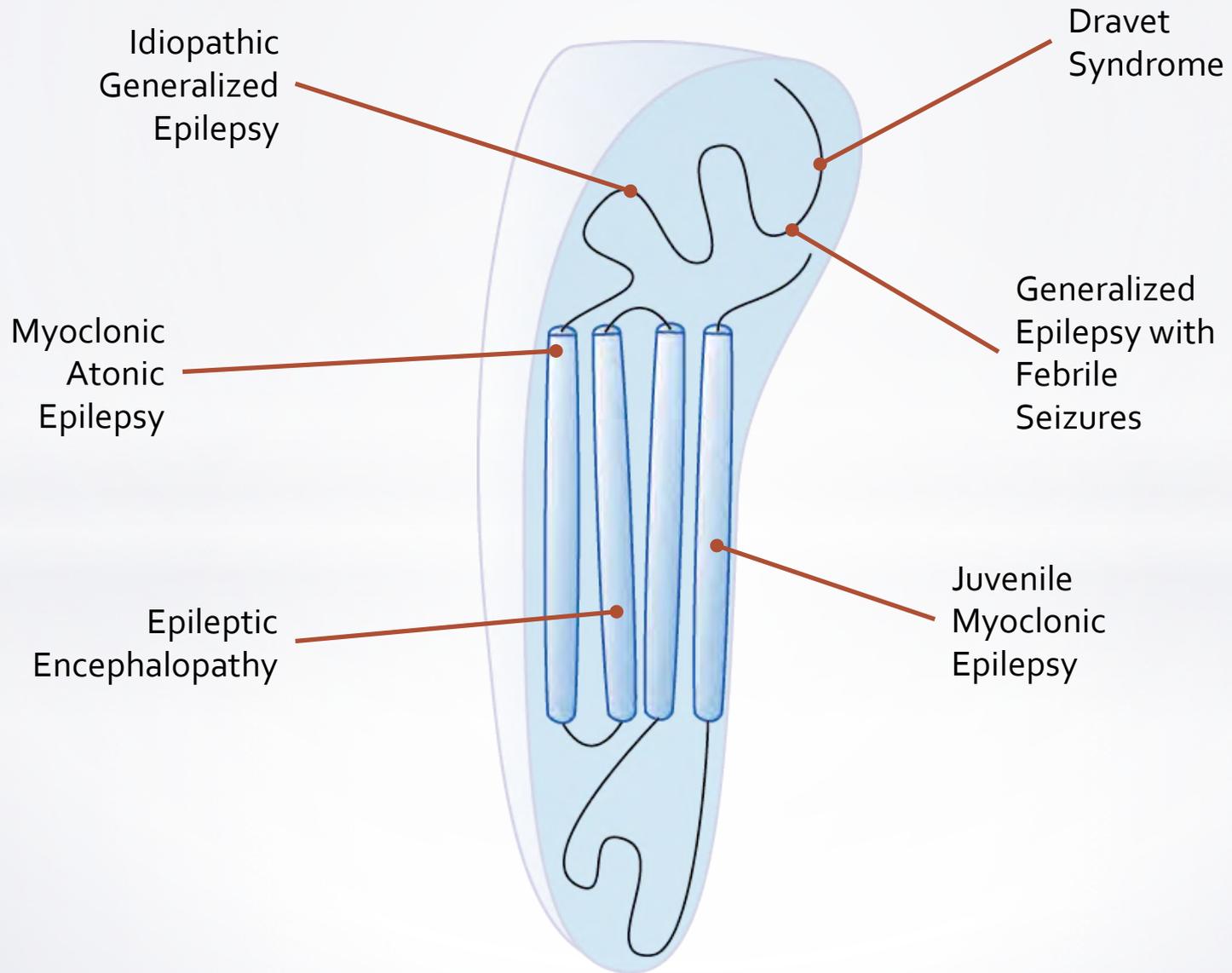
CBD



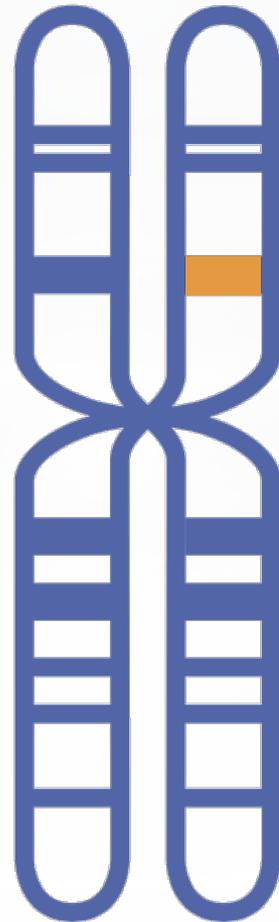
CBN



# GABRA1



[loxP:gabra1]



# PATIENTS



PATIENT



GENE



MODEL



DRUG



# PRECISION MEDICINE DE PRÉCISION



# THANKS



Raphaëlle  
Riché



Amrutha Swaminathan



Lee Ellis  
Fabrice Berthé



Patrick Cossette  
Caroline Méloche  
Louis-Charles Levros  
Brianna Goldenstein



Patrick Gendron  
Florent Guilloteau



Université  
de Montréal



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MECHANISMS**  
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