

GEAI 2012



LES SYNAPTOPATHIES AUTOIMMUNES

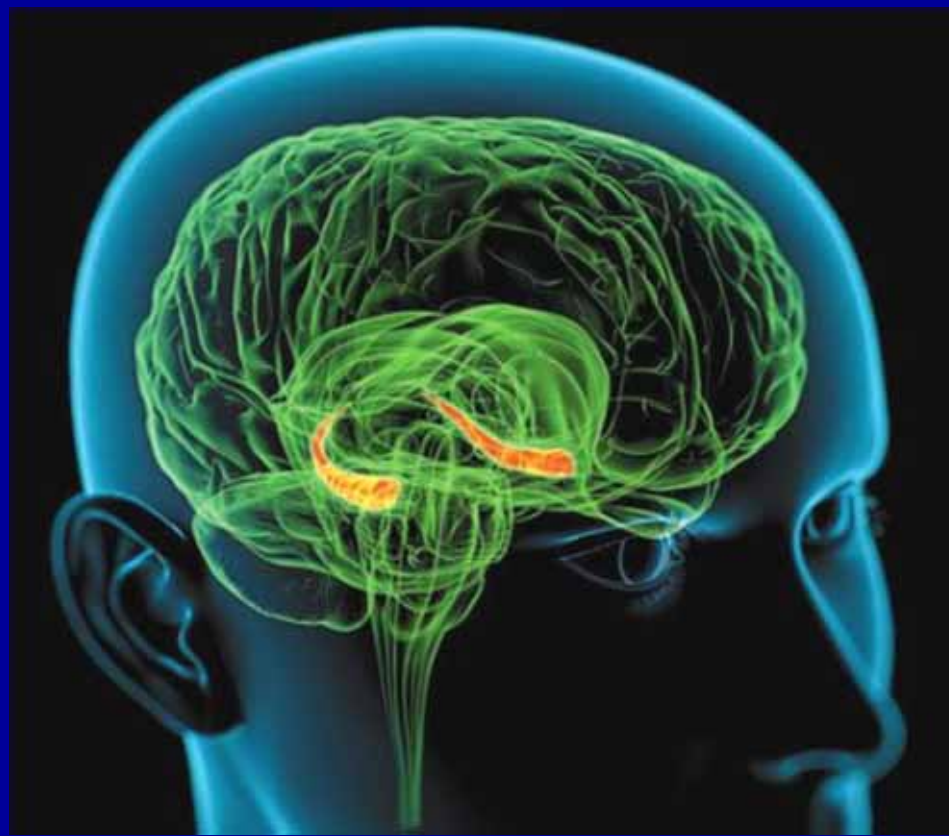
René Louis Humbel
Sylvie Coito
Ghislaine Foerster
Iulia Hila
Myriam Toussaint



SYNAPSES



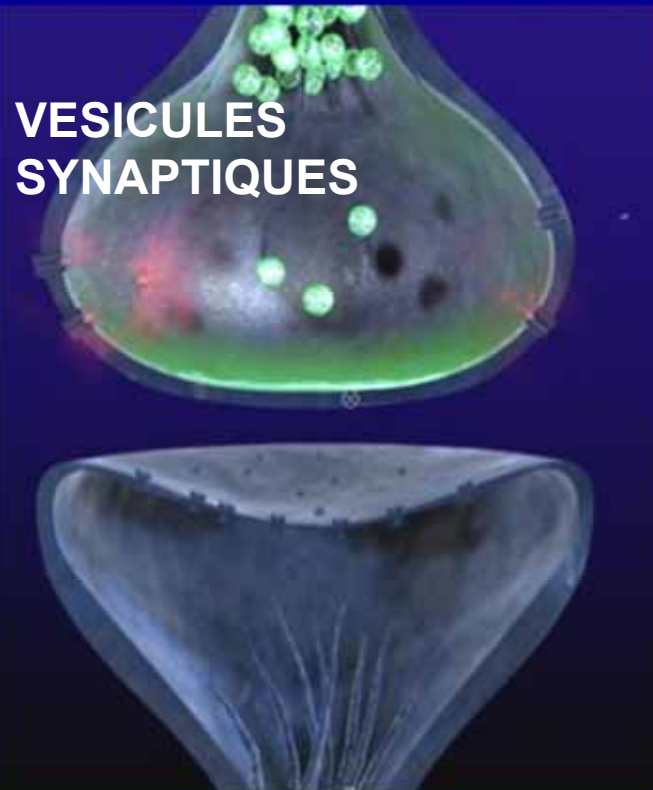
SYNAPTOPATHIES



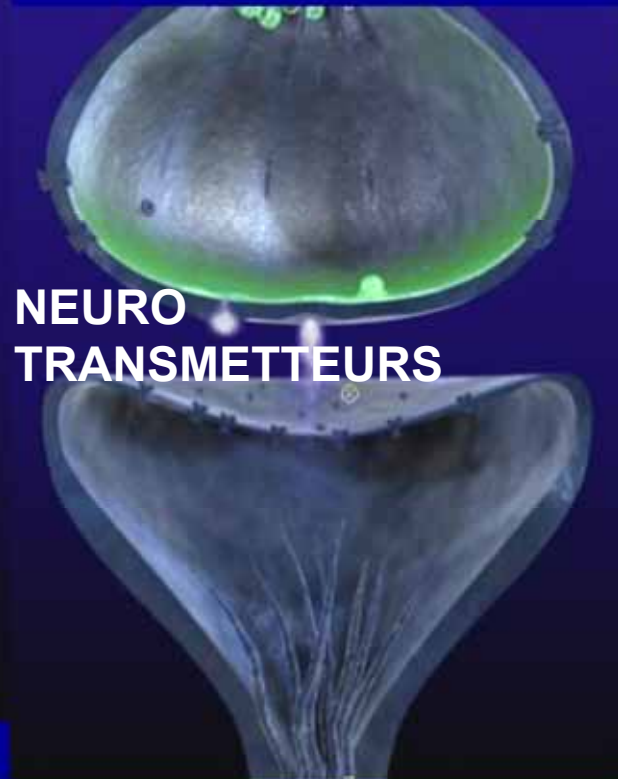
AUTOANTICORPS

La Transmission Synaptique

ELEMENT PRESYNAPTIQUE



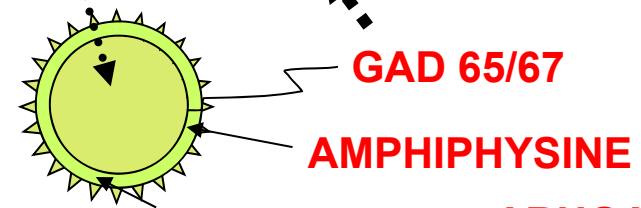
FENTE SYNAPTIQUE



ELEMENT POSTSYNAPTIQUE

ELEMENT PRE-SYNAPTIQUE

GABA ← GLUTAMATE



VESICULES SYNAPTIQUES

Contactine 2

Caspr2

ADAM23

Lgi1

ADAM22

RECEPTEUR GLUTAMATE AMP

RECEPTEUR GLUTAMATE mGluR1

HOMER3

RECEPTEUR GLYCINE

GEPHYRINE

RECEPTEUR GLUTAMATE mGluR5

RECEPTEUR GLUTAMATE NMDA

RECEPTEUR GLUTAMATE GABA B

VGKC

VGKC

ELEMENT POST-SYNAPTIQUE

PROTEINES MEMBRANAIRES

CANAUX IONIQUES

VGCC
VGKC

RECEPTEURS SYNAPTiques

MDAR-GluR (NR1/2)
AMPA-GluR (GluR1/2)
mGluR1
GluR2 δ (NR2B)
GABA R (B1,B2)
Glycine R

PROTEINES SYNAPTiques

Amphiphysine
HOMER 3
(mGluR1)
Caspr 2
Lgi1
(VGKC Kv1)
Géphyrine
(GlycineR)

ENCEPHALITE LIMBIQUE

SYMPTOMATOLOGIE NEURO-PSYCHIATRIQUE SUBAIGUE PROGRESSIVE



TROUBLES COGNITIFS

Perte de la Mémoire Antérograde
Confusion Mentale

SYNDROME PSYCHIATRIQUE

Psychose, Dépression, Anxiété, Agitation
Hallucinations, Confusion, Démence

CRISES D'EPILEPSIE

Epilepsie temporale, Convulsions
Pharmaco-résistantes

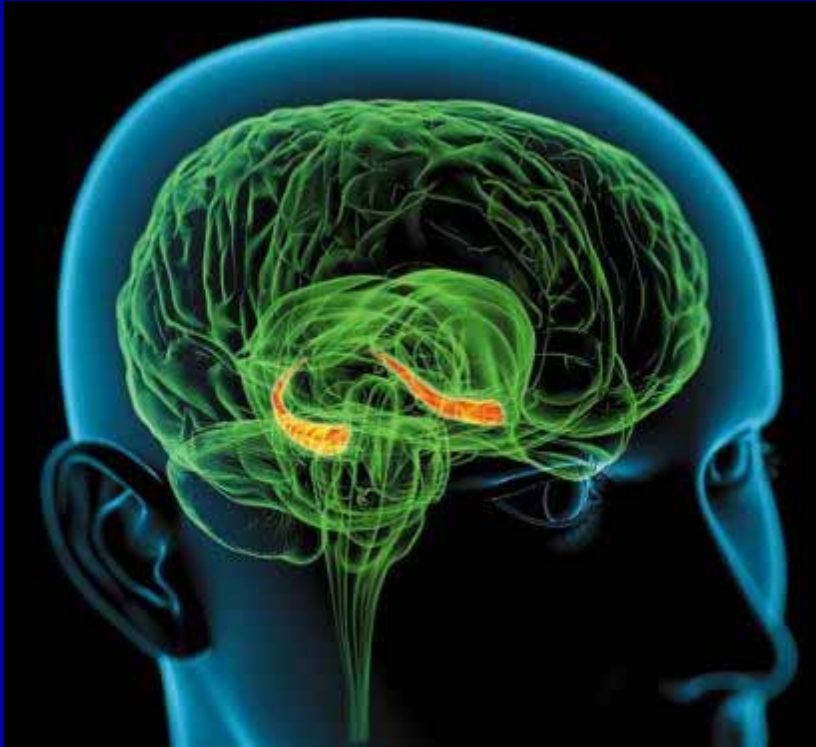
CONTRACTIONS MUSCULAIRES

Dystonie, Myoclonies,
Dyskinésie orofaciale
Rigidité Musculaire

ATTEINTES HYPOTHALAMIQUES

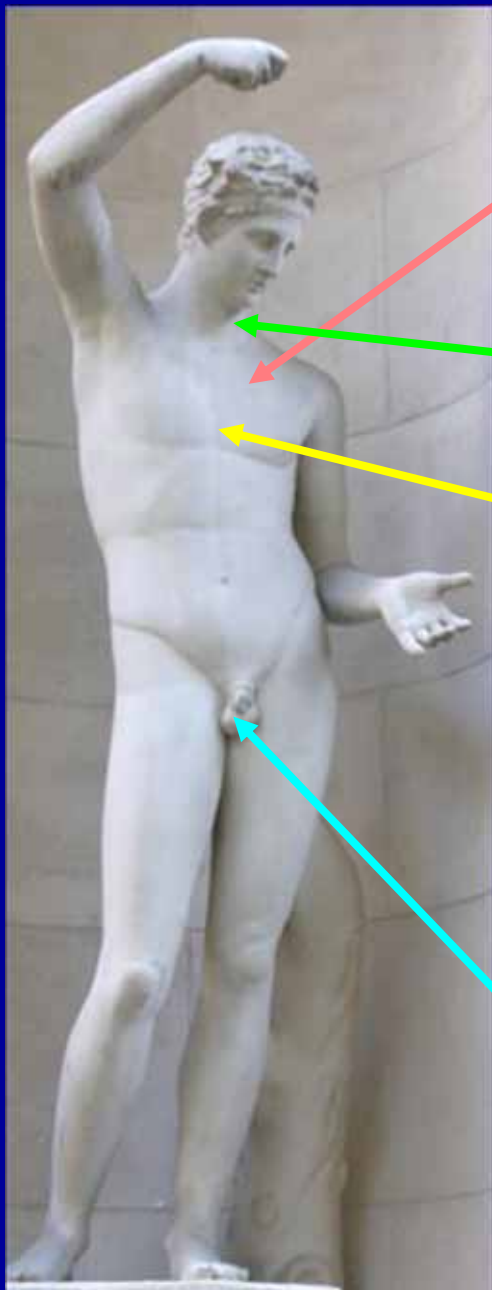
Hyperthermie, Dysautonomie,
Narcolepsie, Hyponatrémie

ENCEPHALITE LIMBIQUE



**Sujets Agés , Jeunes
Enfants**

**IDIOPATHIQUE
PARANEOPLASIQUE**



**CANCER PULMONAIRE
PETITES CELLULES**

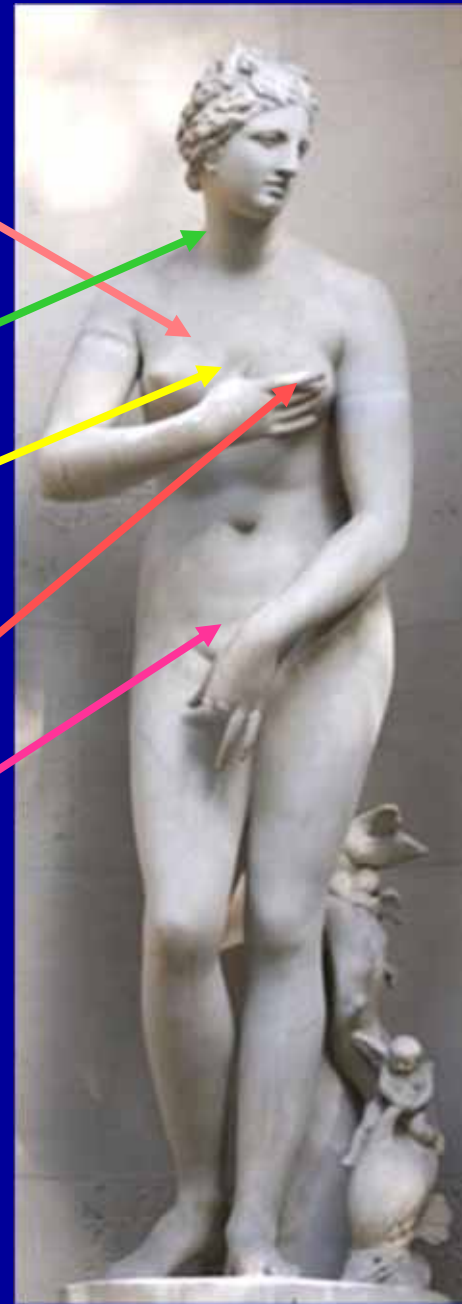
HODGKIN

THYMOME

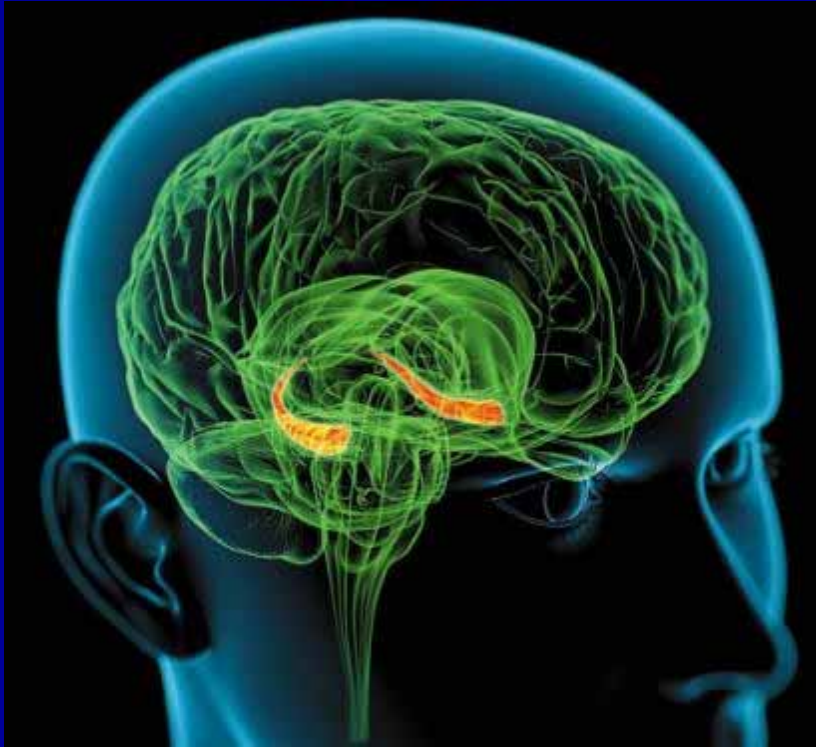
SEIN

OVAIRE

TESTICULES



ENCEPHALITE LIMBIQUE



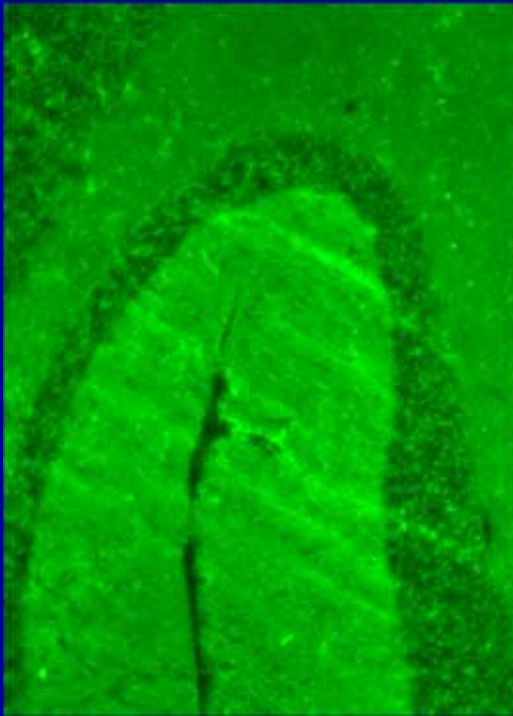
**Sujets Agés , Jeunes
Enfants**

IMMUNOTHERAPIES

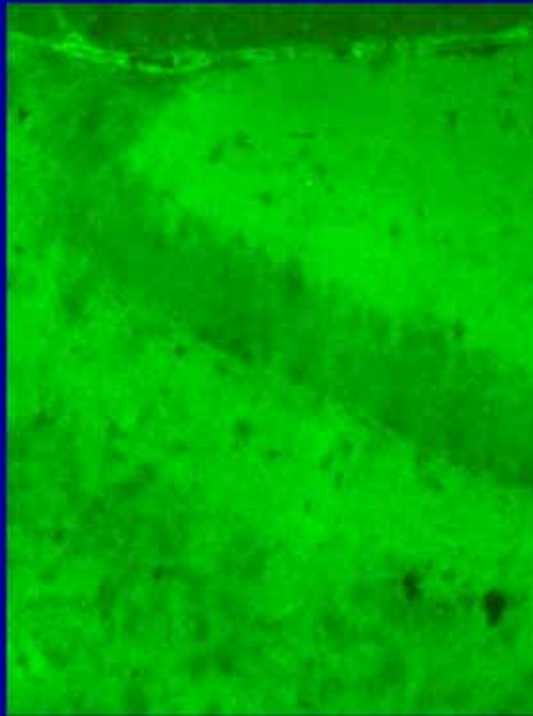
RECHERCHE ET IDENTIFICATION DES ANTICORPS

IMMUNOFLUORESCENCE

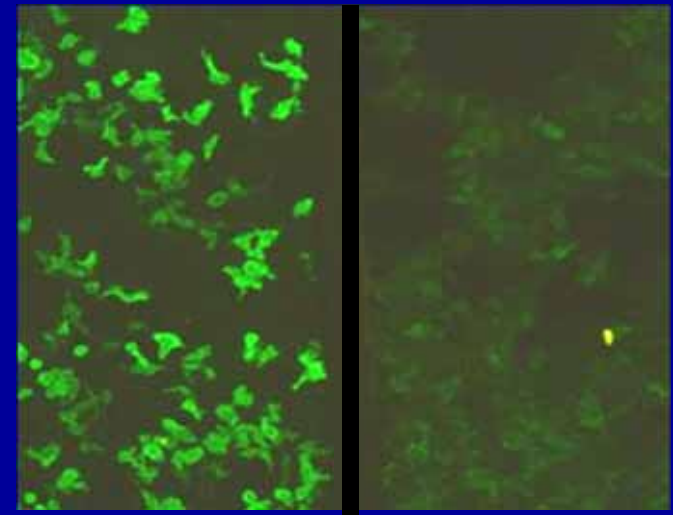
CERVELET



HYPPOCAMPE



CELLULES
TRANSFECTEES



NMDAR , AMPAR , GABA_b ,
Lgi1 , Caspr2 , GlyR

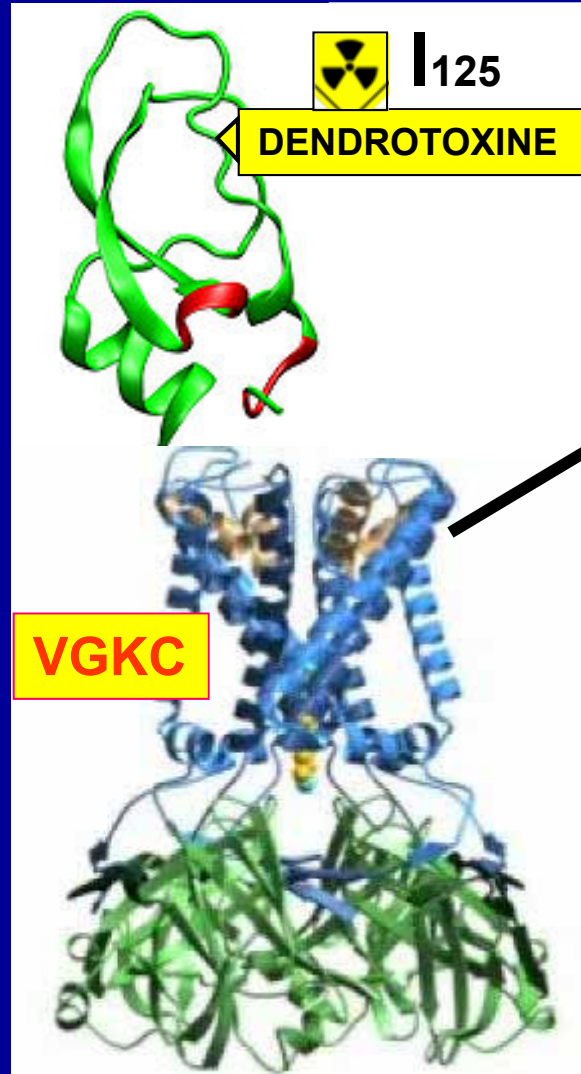
Couche Moléculaire



CERVEAU RAT

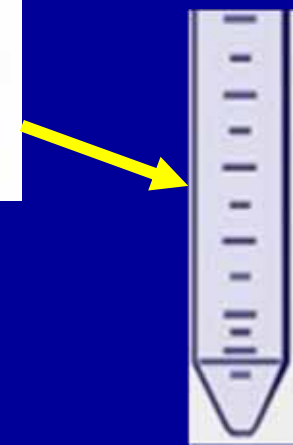


EXTRACTION DES MEMBRANES



MARQUAGE VGKC Kv1

Cell-adhesion molecules	<u>Caspr-2</u>
	<u>contactin1</u>
Transporters	Na/K-ATPase (α, β)
	Ca-ATPase (plasma membrane)
Synaptic proteins	syntaxin binding protein 1
	syntaxin 1b
	synaptotagmin P65
	synapsin 1b
Proteins of unknown function	<u>LGI1</u>
	ADAM22
	GIT1

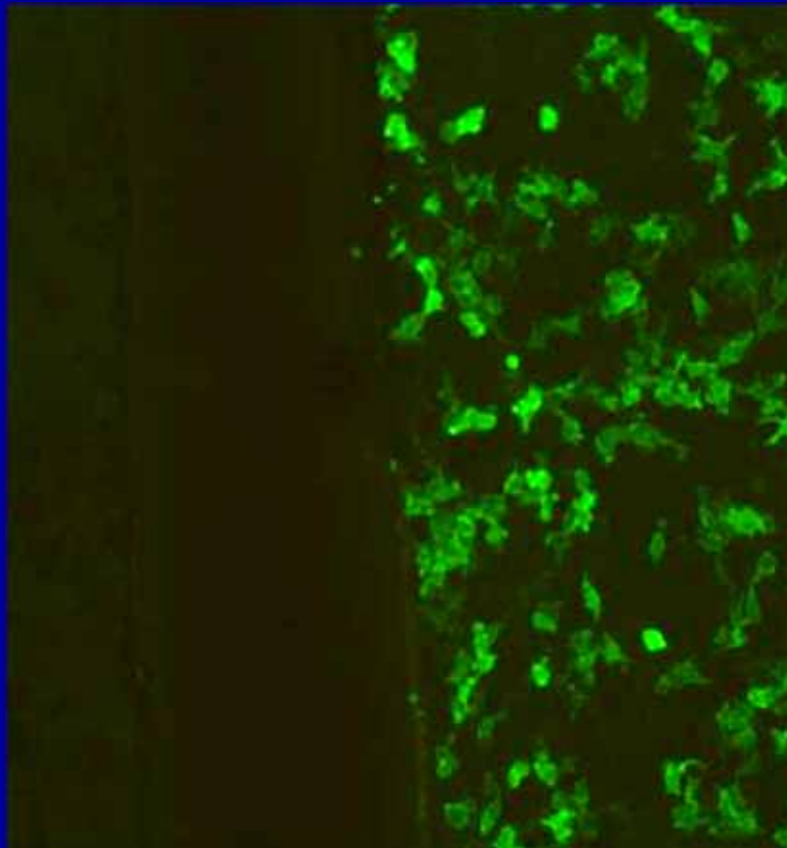


RADIOIMMUNOPRECIPITATION

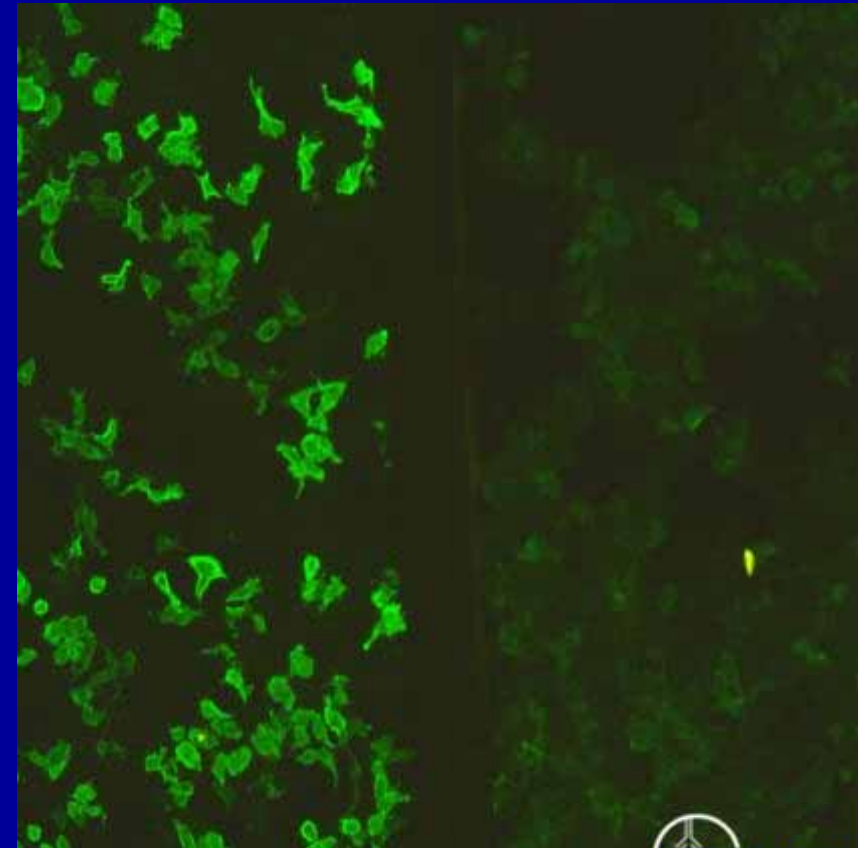
ANTICORPS ANTI-VGKC

Cellules Transfectées

Lgi1



Caspr2



ANTICORPS ANTI-VGKC

Kv1.1

Epilepsie

Lgi1

**Troubles Sommeil
Dystonie Facio-brachiale
Mnésie Sévère
Convulsions
Epilepsie**

Caspr2

**Hyperexcitabilité
neuromusculaire
Crampes
Fasciculations
Hallucinations
Délire
Mnésie**

Tumeur

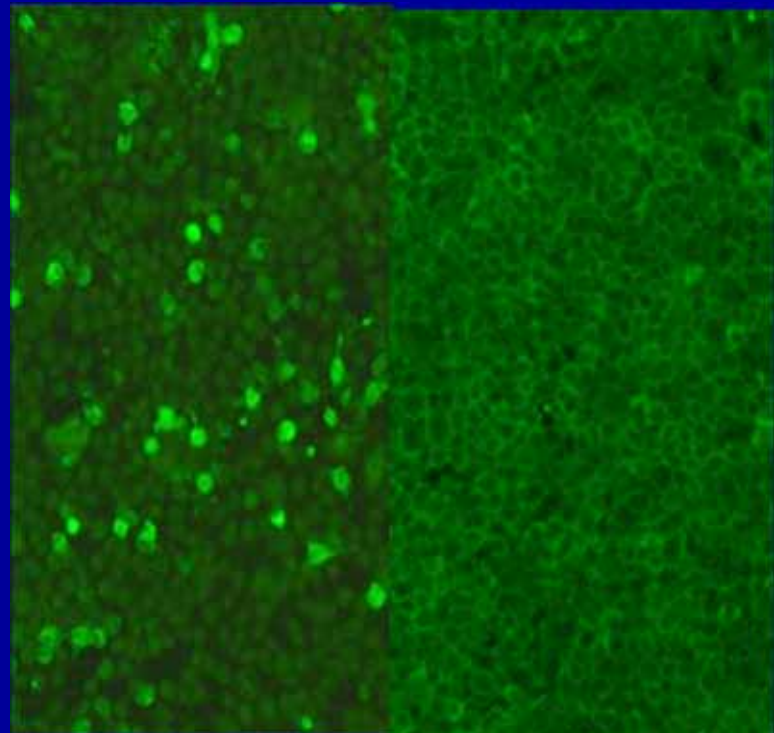
ANTICORPS ANTI-Glu NMDAR

Dyskinésie Orofaciale
Posture Dystonique
Désintégration du Langage
Epilepsie
Catatonie

Jeunes Femmes
Enfants

Tératome Ovarien

IF Cellules Transfectées



ANTICORPS ANTI-Glu AMPAR

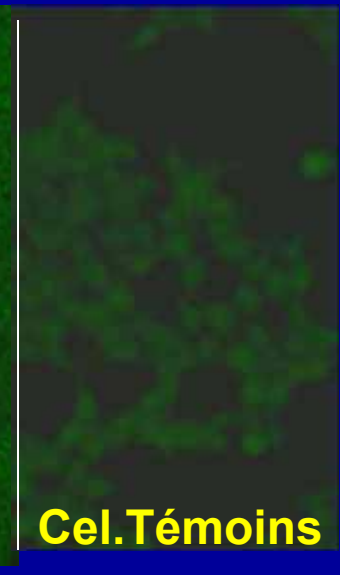
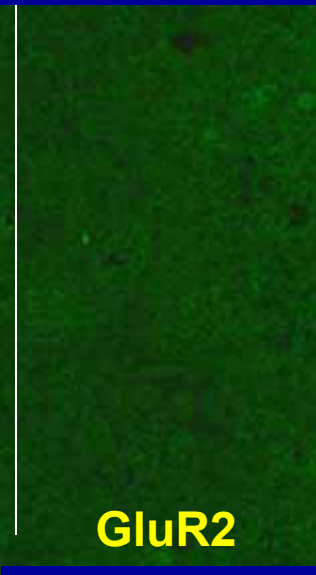
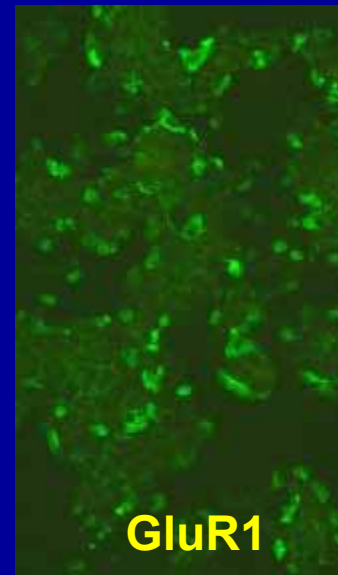
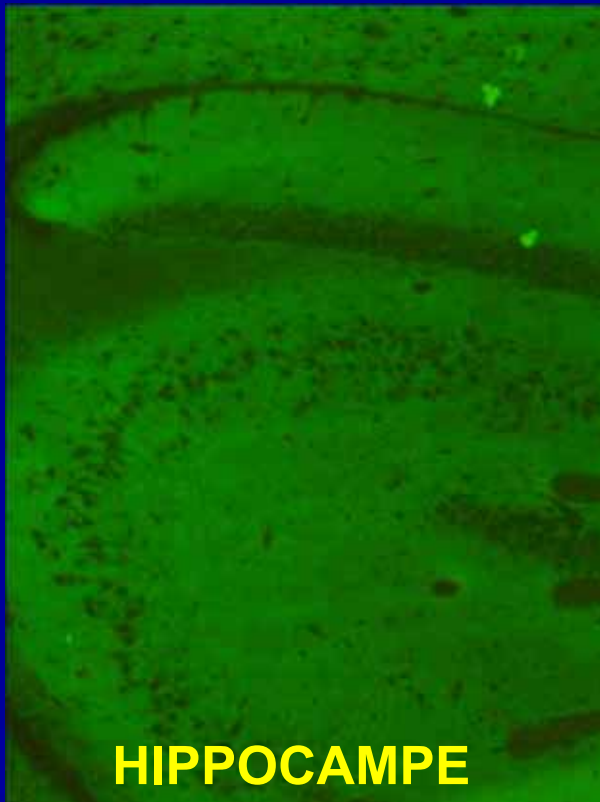
Perte de mémoire
Confusion, Agitation
Convulsions

80% Femmes

Cancer du Sein,
Thymus, Poumon

IF Cellules Transfectées

Sous unités GluR1/R2



ANTICORPS ANTI – mGluR1

**Cytoplasme des Cellules
de Purkinje**

**Couche Moléculaire
Finement granulaire**

**mGluR1 : metabotropic
glutamate Receptor 1**

**DEGENERESCENCE
CEREBELLAIRE**

MALADIE de HODGKIN

mGluR1



ANTICORPS ANTI - GluR2 δ

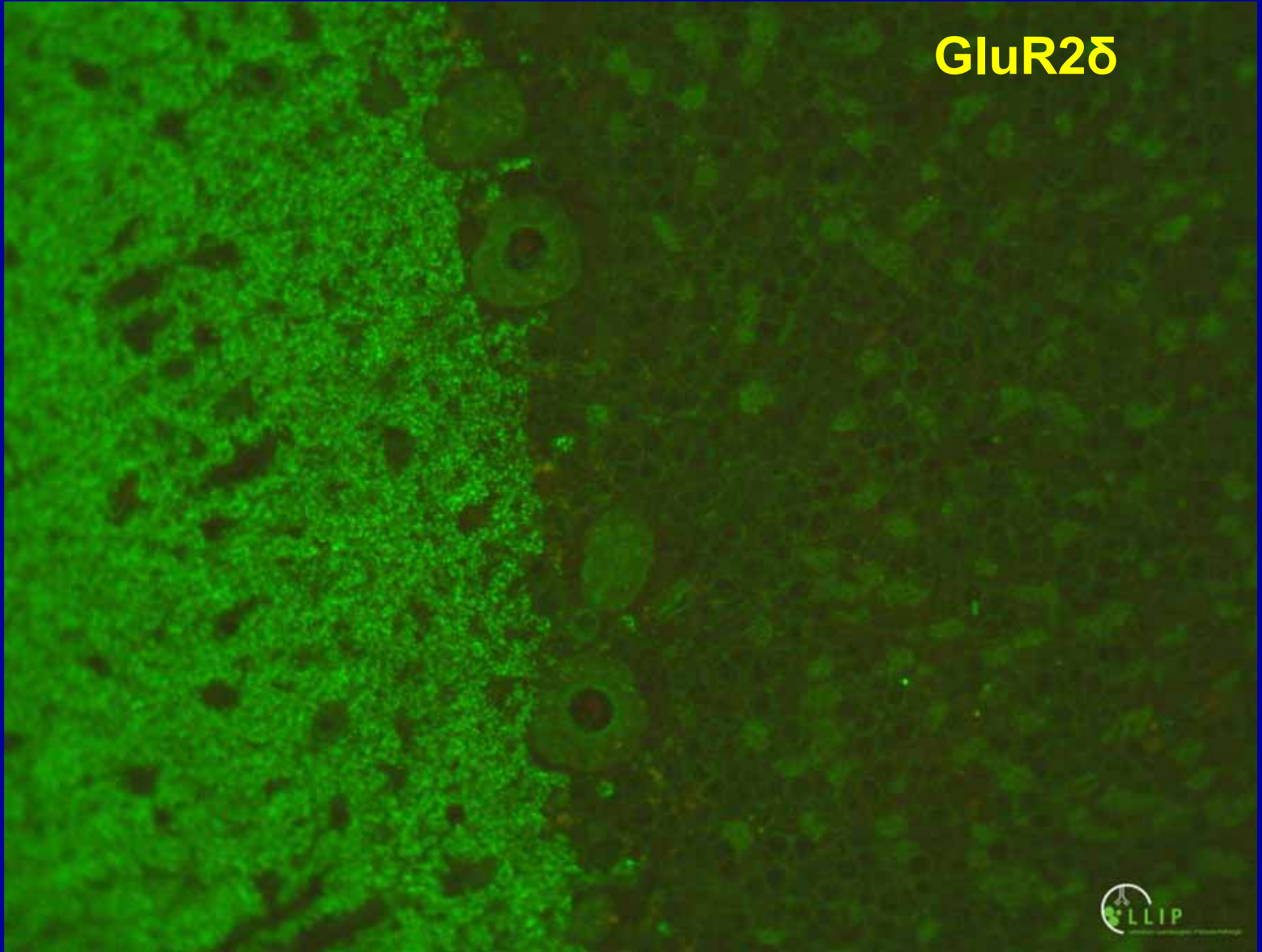
COUCHE MOLECULAIRE
GRANULAIRE

Glutamate Receptor 2 δ

ATAXIE CEREBELLEUSE

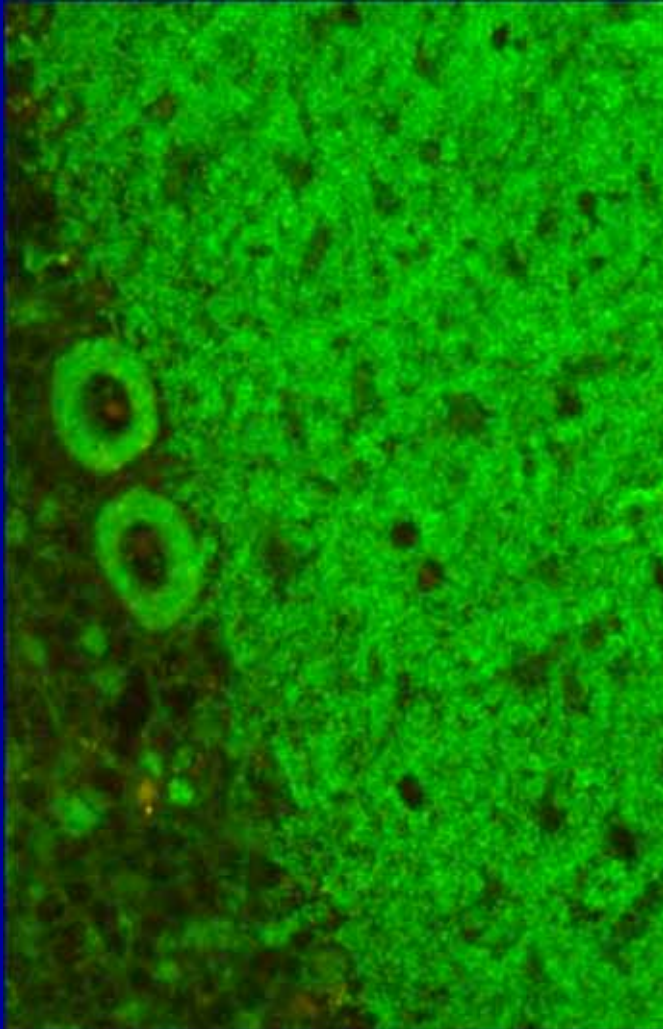
MALADIE de HODGKIN

GluR2 δ

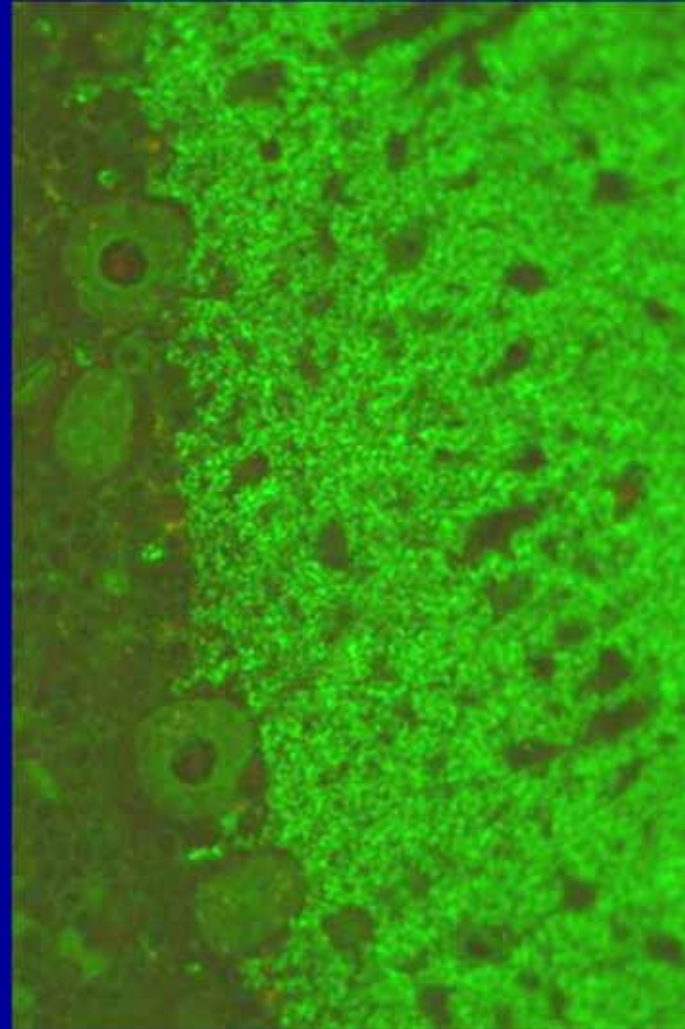


ANTICORPS ANTI-GluR

mGLUR1



GLUR2 δ



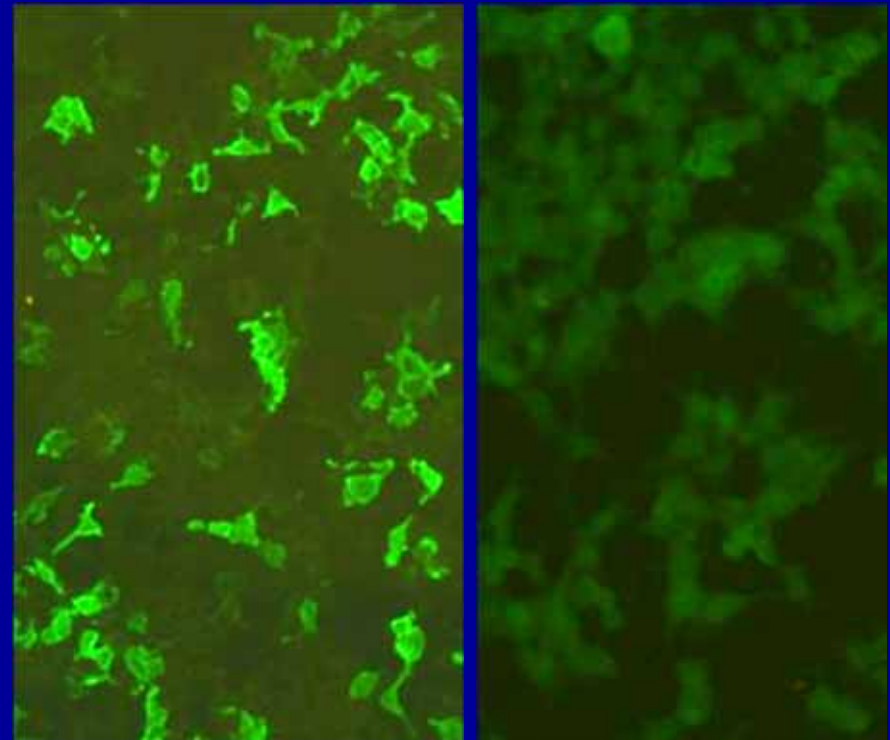
ANTICORPS ANTI-GABA R

**Epilepsie
Psychose, Hallucinations,
Agressivité
Troubles du sommeil**

**Cancer Pulmonaire
microcellulaire**

50% associés avec Anti-GAD !!

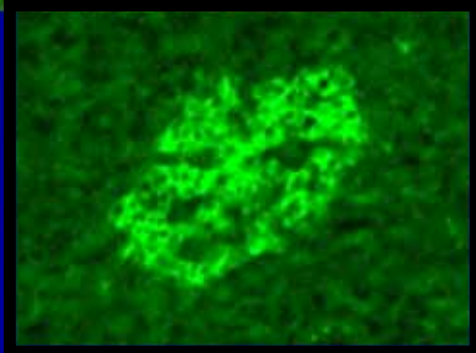
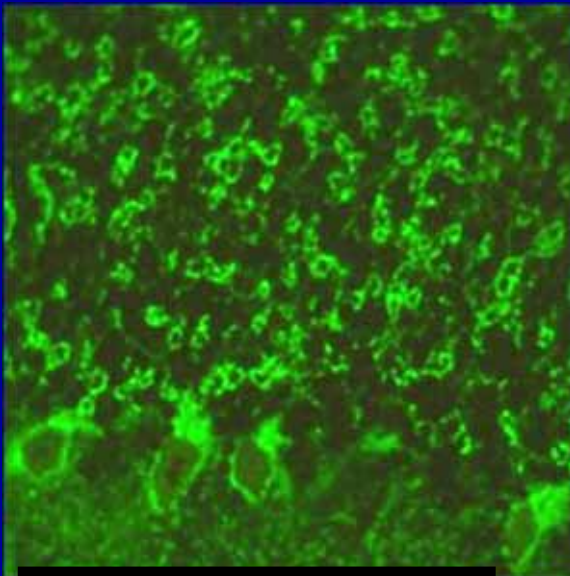
IF Cellules Transfectées



RIGIDITE MUSCULAIRE

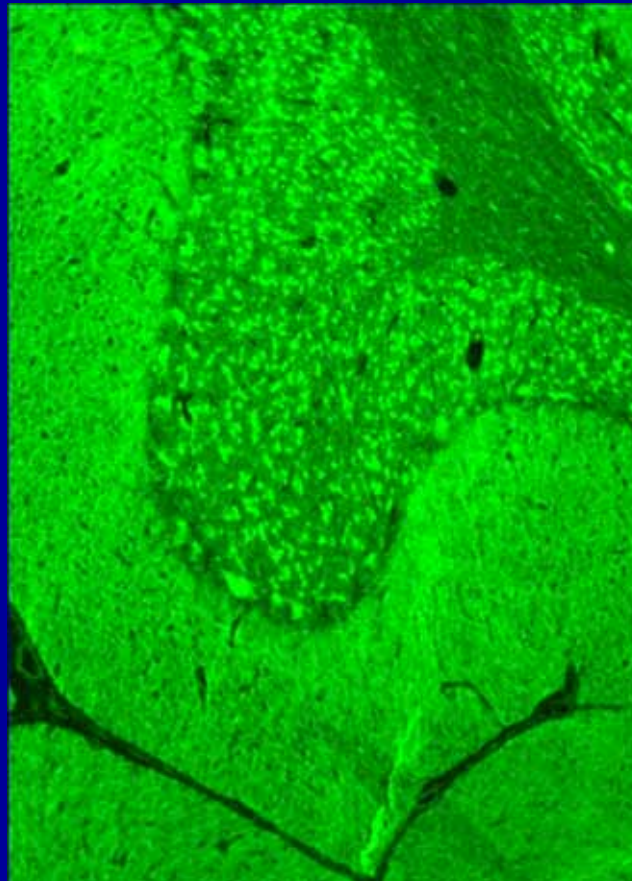
GAD

Ataxie
Encéphalomyélite
Epilepsie



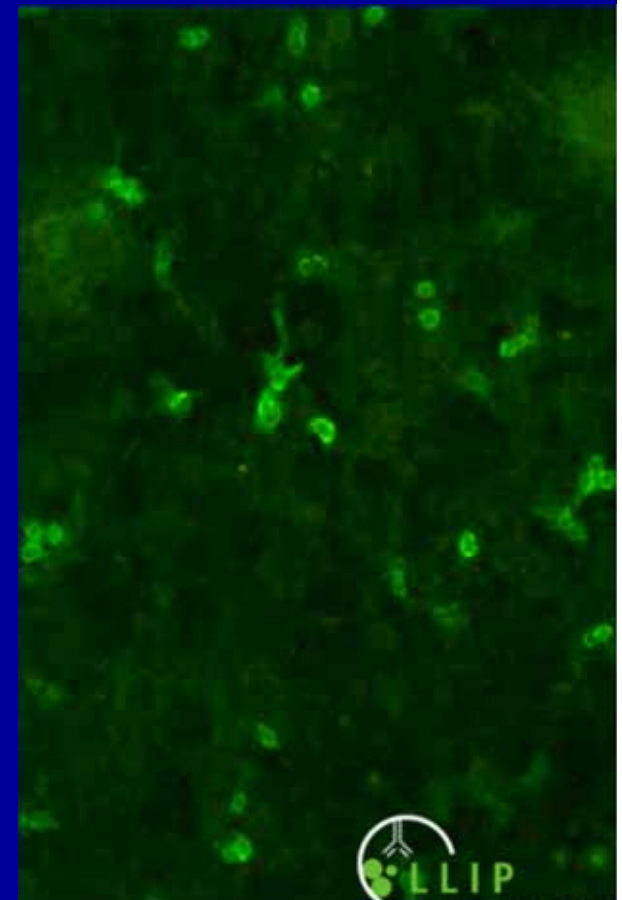
AMPHIPHYSINE

Ataxie
Encéphalomyélite



RECEPTEUR GLYCINE

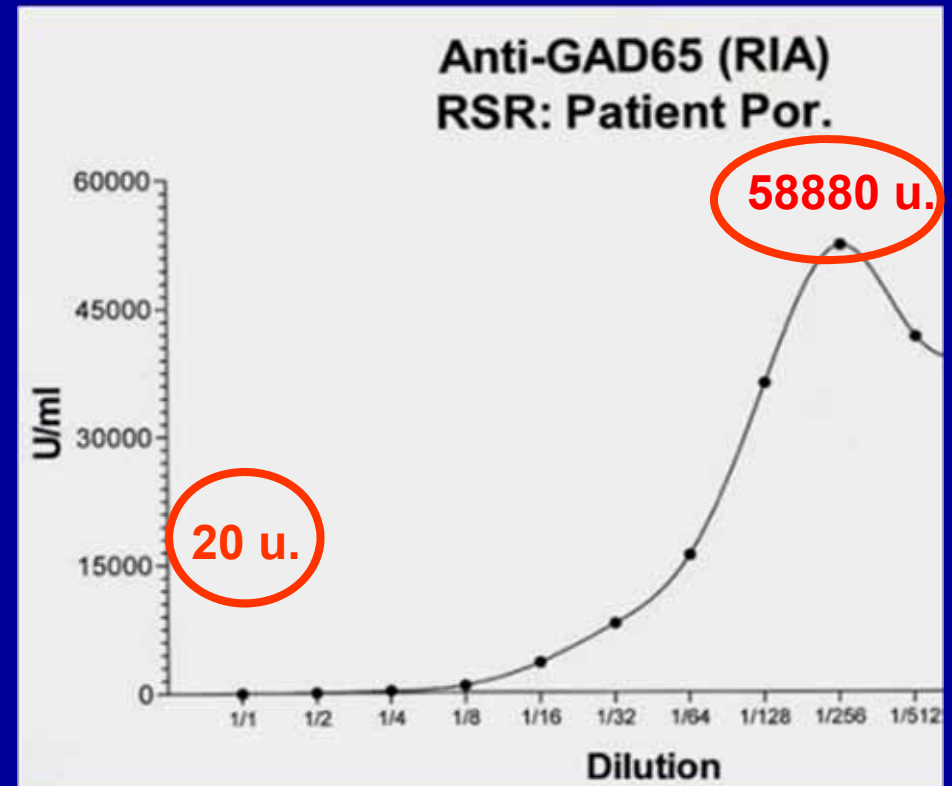
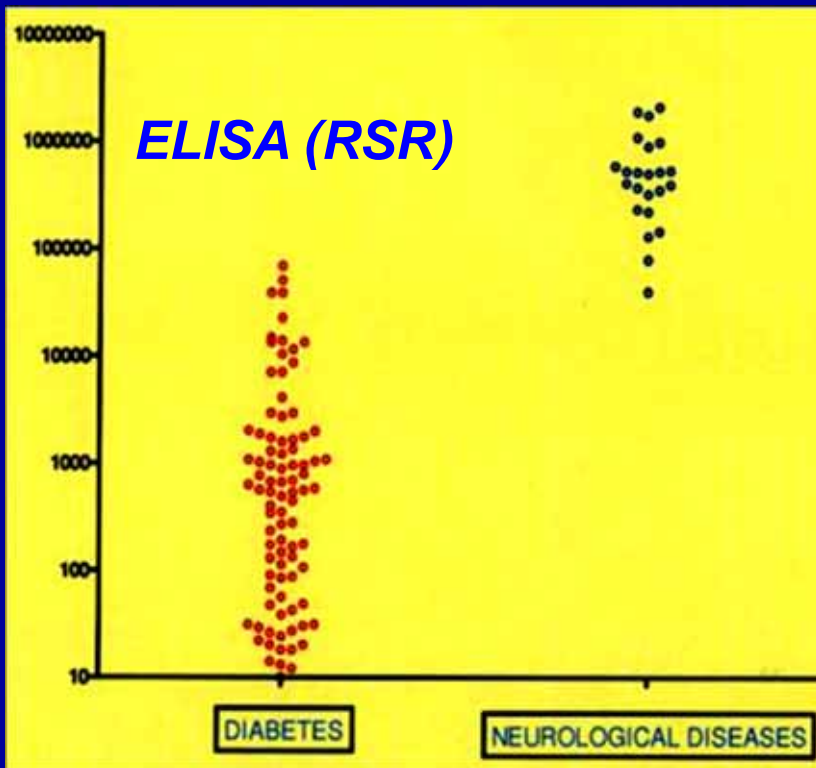
Epilepsie



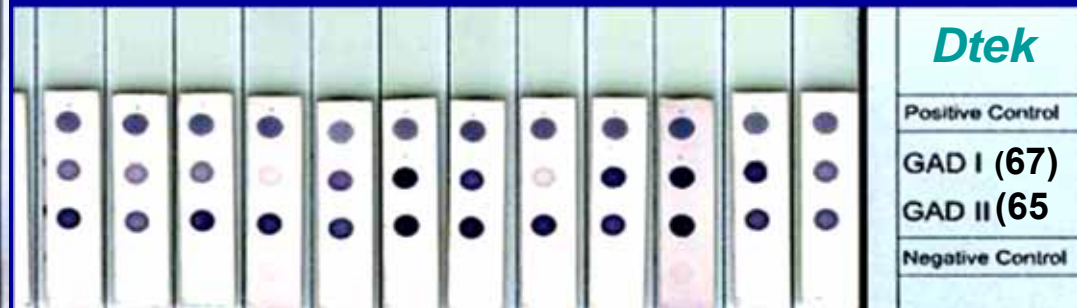
ANTI - GAD

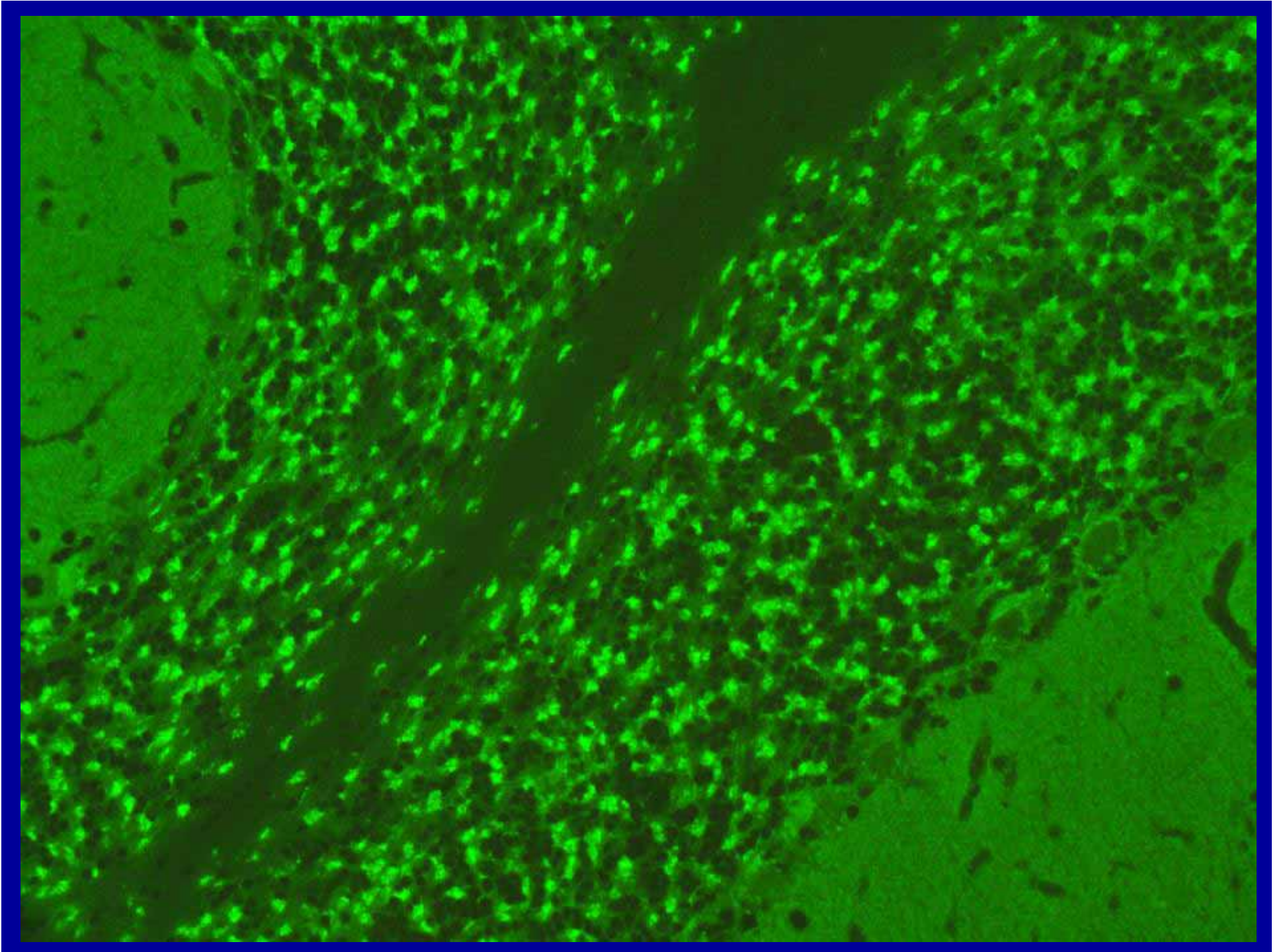
CERVELET

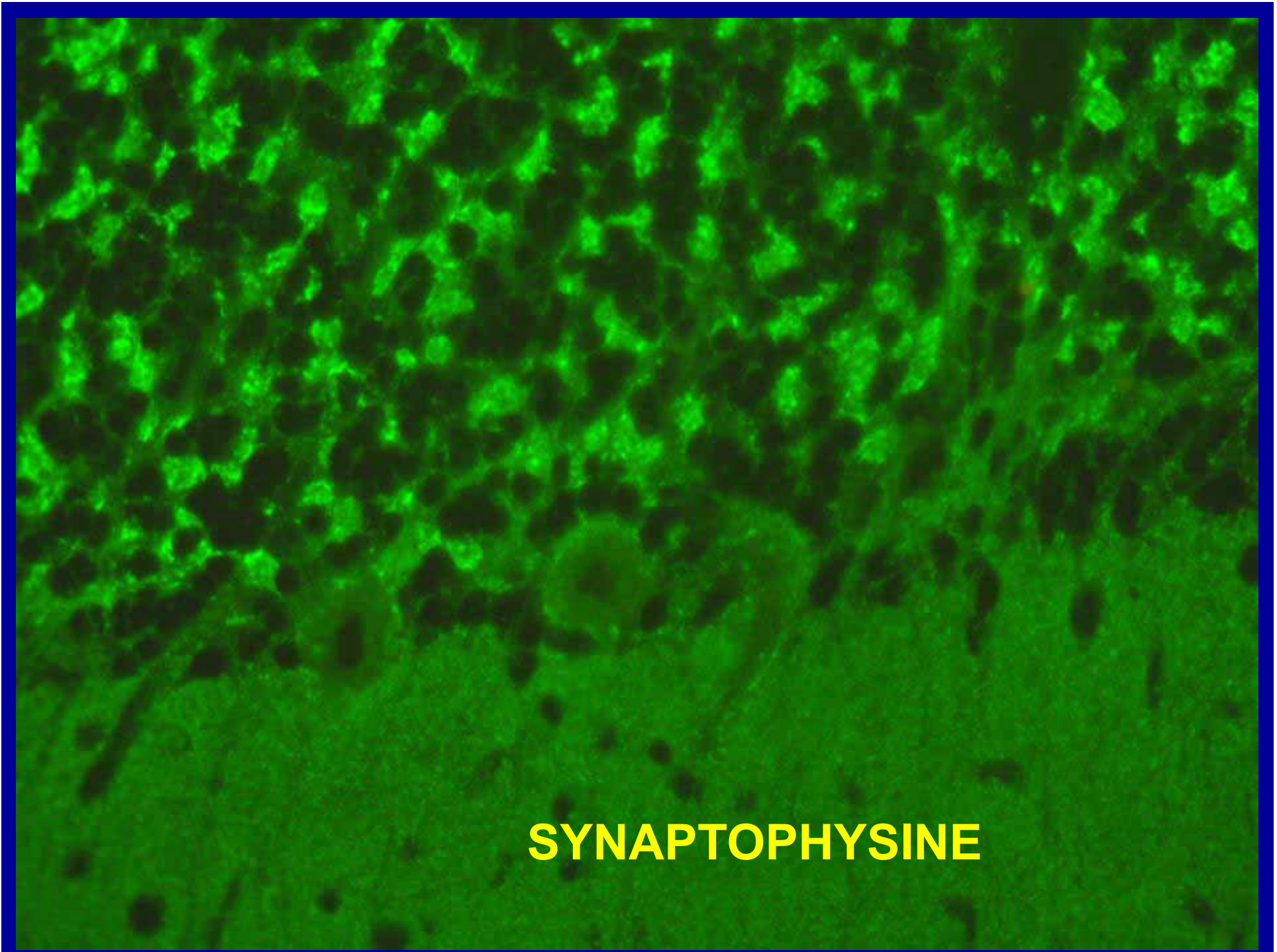
ANTI-GAD 65 ANTIBODIES



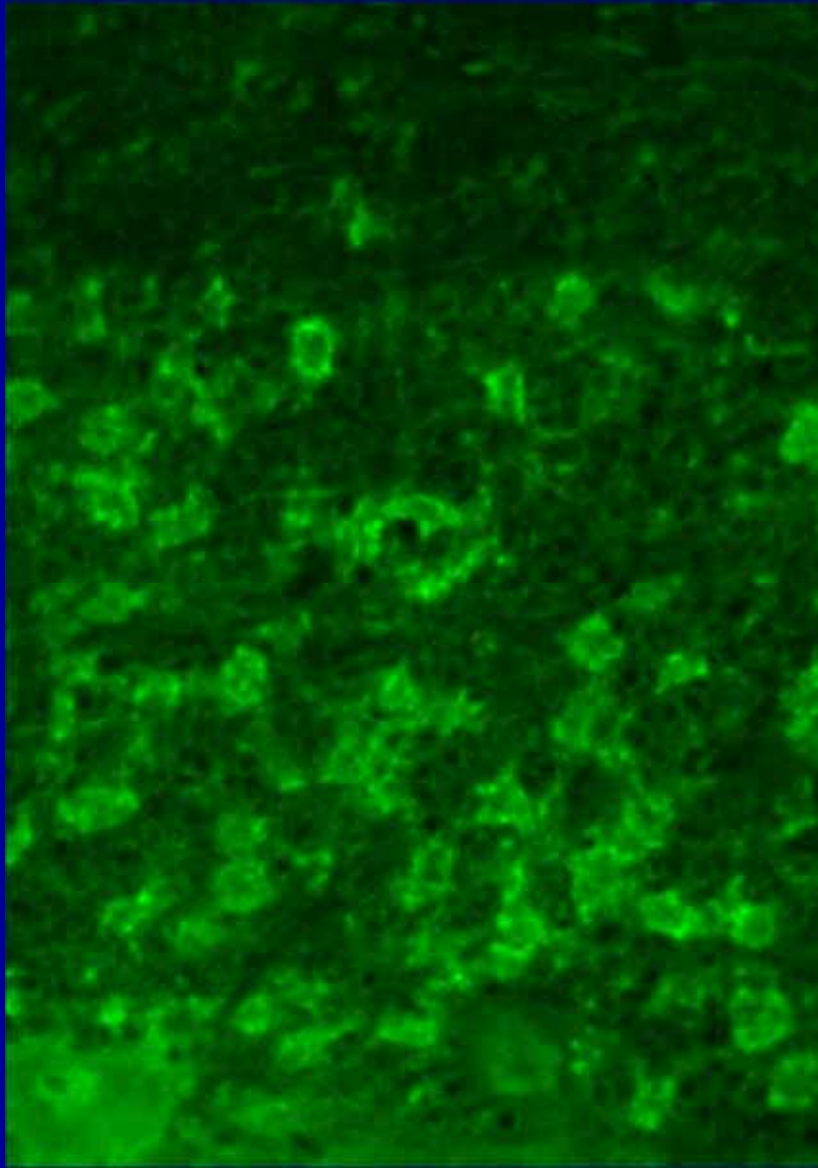
IMMUNODOT



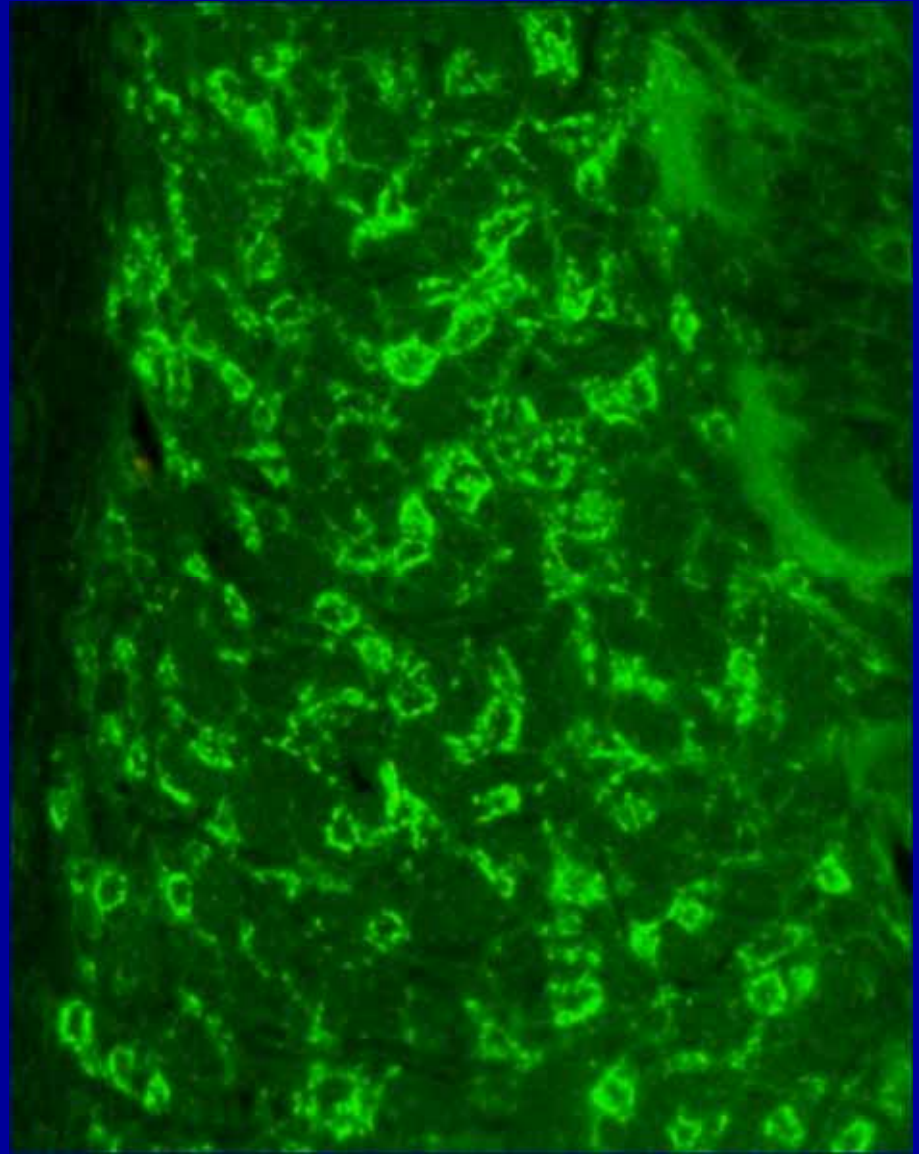




SYNAPTOPHYSINE



SYNAPTOPH.



GAD

