

REVUE SUR LES AUTOANTICORPS ANTI - NEURONAUX



René-Louis HUMBEL



AUTOIMMUNE DISEASES
OF THE NERVOUS SYSTEM

PARANEOPLASTIC

IDIOPATHIC



IMMUNOFLUORESCENT DETECTION OF ANTIBODIES
AGAINST NEURONES IN SENSORY CARCINOMATOUS
NEUROPATHY

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Brain, 1965

ANTIBODIES To

Yo	1983	ANNA-3	2001
Hu	1985	Zic	2002
GAD	1988	SOX	2005
VGCC	1989	BRSK2	2005
Ri	1991	GluR2 δ	2005
VGKC	1995	PKC γ	2006
CV2	1996	HOMER 3	2007
AMPHI	1993	AK5	2007
Tr	1997	NMDAR	2007
Ma/Ta	1999	GlycineR	2008
mGluR1	2000	CASPR2	2009
PCA-2	2000	AMPA	2009
Gephyrin	2000	GABA _B R	2010
		ARMGAP26	2010
		Lgi1	2010




BRSK2	Brain Specific Serine-Threonine Kinase
PKCγ	Protein-Kinase gamma
HOMER 3	Protein Homer 3
AK5	Adenylate-Kinase 5
NMDAR	N-methyl-4-isoxazole prpopionic acid GluR
CRMP3	Collapsin Response Mediator Protein 3
CASPR2	Contactin Associated Protein 2
AMPA	N-methyl-D-aspartate GluR
ARHGAP26	RhoGTPase Activating Protein 26
Lgl1	Leucine-rich glioma inactivated gene 1



AUTOANTIBODIES TO CENTRAL NERVOUS SYSTEM

INTRANEURONAL ANTIGENS	NEURONAL CELL SURFACE RECEPTORS, ION CHANNELS SYNAPTIC PROTEINS
NEURONAL NUCLEI : Hu,Ri,,Zic,Sox	VGCC
NEURONAL NUCLEOLI : Ma1, Ma2/Ta	VGKC,Lgi1,Caspr2
NEUR.CYTOPLASM : BRSK 2,AK5,GAD	AMPA-GluR
PURKINJE CYTOPL : Yo,PCA2,Tr,PKCY	NMDAR-GluR
PURKINJE NUCLEI : ANNA3	mGluR1m, Homer 3
OLIGODENTROCYTES : CV2	GluRδ2
	GABA R B1
	GlycineR , Gephyrine
	Aquaporin- 4
	Amphiphysin



ANTIBODIES TO INTRA-NEURONAL ANTIGENS

NEURONAL NUCLEI / CYTOPLASM : Hu,Ri

NEURONAL NUCLEI : Zic

NEURONAL NUCLEOLI : Ma/Ta

NEURONAL NUCLEI / GLIAL CELLS : Sox

NEUR.CYTOPLASM : BRSK 2,AK5, GAD

PURKINJE CYTOPL : Yo,PCA2,Tr, Ca ,PKC γ

PURKINJE NUCLEI : ANNA3

OLIGODENTROCYTES CYTOPLASM : CV2



NEURONAL AUTOIMMUNE DISORDERS OF THE CNS

INTRANEURONAL ANTIBODIES

Encephalomyelitis
Cerebellar Degeneration
Ataxia
Stiff-person Syndrome

NEURONAL SURFACE ANTIBODIES

Limbic Encephalitis
Memory Loss
Psychiatric Changes
Seizures

PARANEOPLASTIC

*PARANEOPLASTIC
OR IDIOPATHIC*



AUTOANTIBODIES TO CENTRAL NERVOUS SYSTEM

INTRANEURONAL ANTIGENS

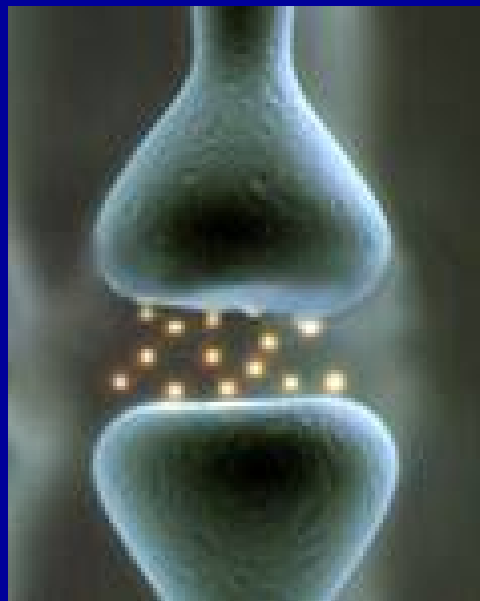
NEURONAL CELL SURFACE RECEPTORS, ION CHANNELS SYNAPTIC PROTEINS

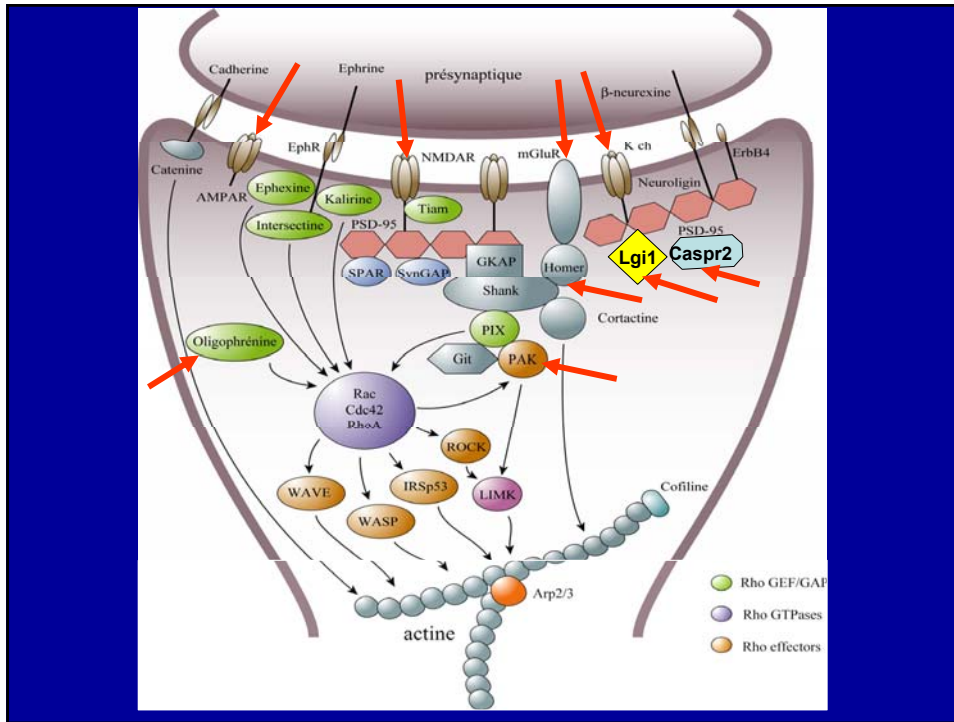
GRANULAR LAYER

MOLECULAR LAYER

- Neurons
- Purkinje Cells
- Oligodendrocytes
- Glial Cells

NEUROPIIL





NEURONAL SURFACE PROTEINS

ION CHANNELS

VGCC
VGKC

SYNAPTIC RECEPTORS

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

SYNAPTIC PROTEINS

HOMER 3
(mGluR1)
Caspr 2
Lgi1
(VGKC Kv1)
Amphiphysin

WATER CHANNEL

Aquaporin 4



SYNAPTIC PROTEINS

RECEPTOR ASSOCIATED PROTEINS

Lgi1 (VGKC)
Caspr 2 (VGKC)
TAG-1 (VGKC)
Gephyrin (Glycin R)

SYNAPTIC VESICLES

Amphiphysin
ARGHGAP26



RAT BRAIN

MEMBRANE EXTRACTION

LABELING VGKC Kv1

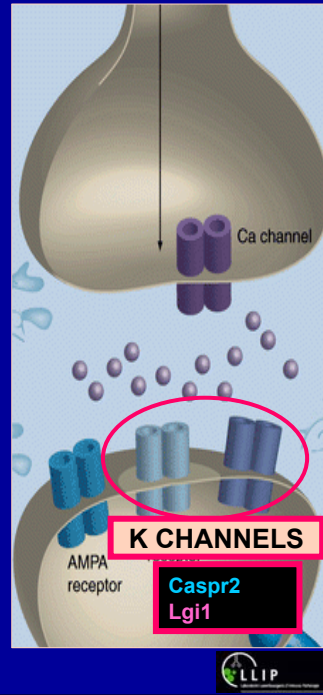
RADIOIMMUNOPRECIPITATION TEST

Cell-adhesion molecules	Caspr-2
Transporters	contactin1
	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	LGI1
	ADAM22
	GIT1

SYNAPTOPATHIES

ANTIBODIES Caspr2 Lgi1

Limbic Encephalitis	40 %	90 %
Morvan's Syndrome	15 %	4 %
Neuromyotonia	4 %	50 %
Seizures	50 %	90 %
Dysautonomia	30 %	15 %
Hyponatremia	10 %	60 %
Active Tumour	30%	0



LIMBIC ENCEPHALITIS

COGNITIVE DYSFUNCTION

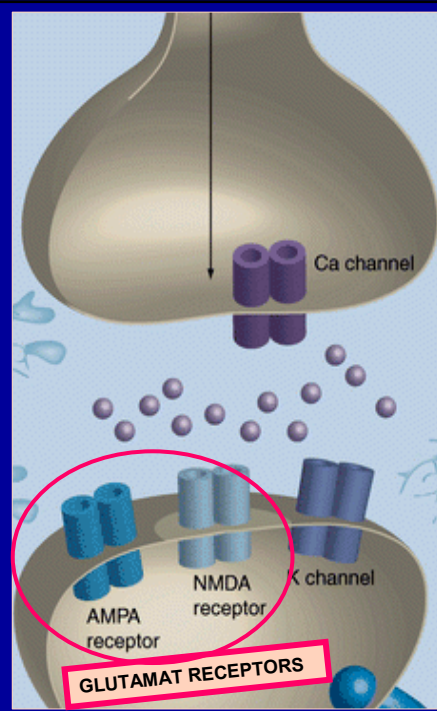
Confusion
Amnesia
Dysphagia
Dyskinesia

PSYCHIATRIC SYMPTOMS

Hallucinations
Psychosis
Anxiety
Agitation
Depression

SEIZURES

OVARIAN TERATOMA
BREAST – LUNG CANCER
THYMOMA



AUTOANTIBODIES TO THE NERVOUS SYSTEM

IMMUNOFLUORESCENCE

Tissue Sections : Brain,Cerebellum,Hyppocampus
Transfected Cells (NMDAR , AQP4 ,Lgi1,Caspr2)

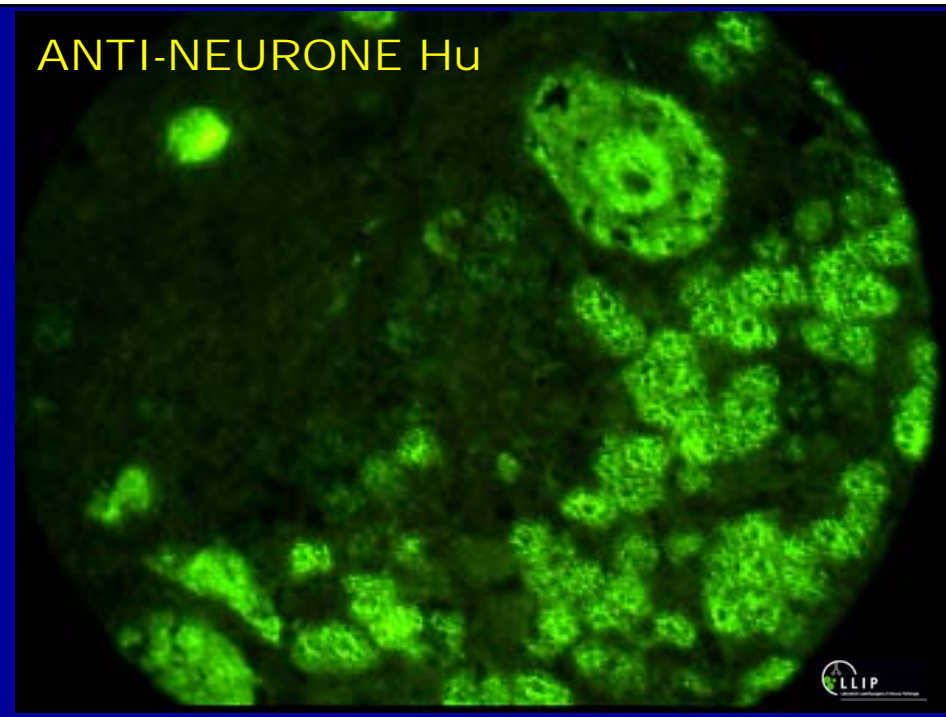
IMMUNODOT **Anti-Neuronal Autoantibodies**

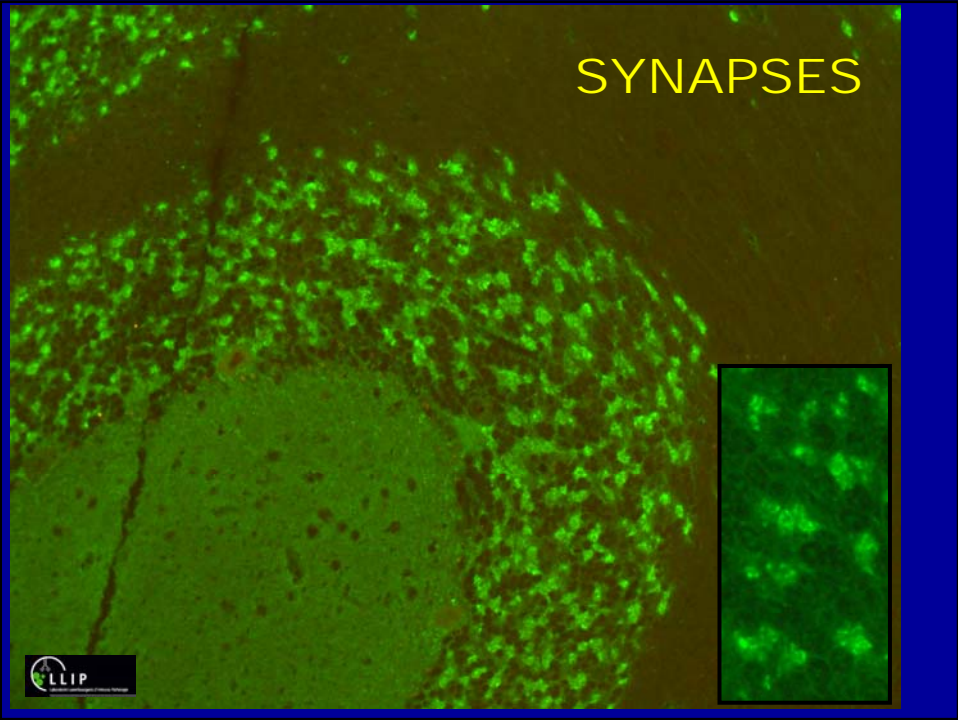
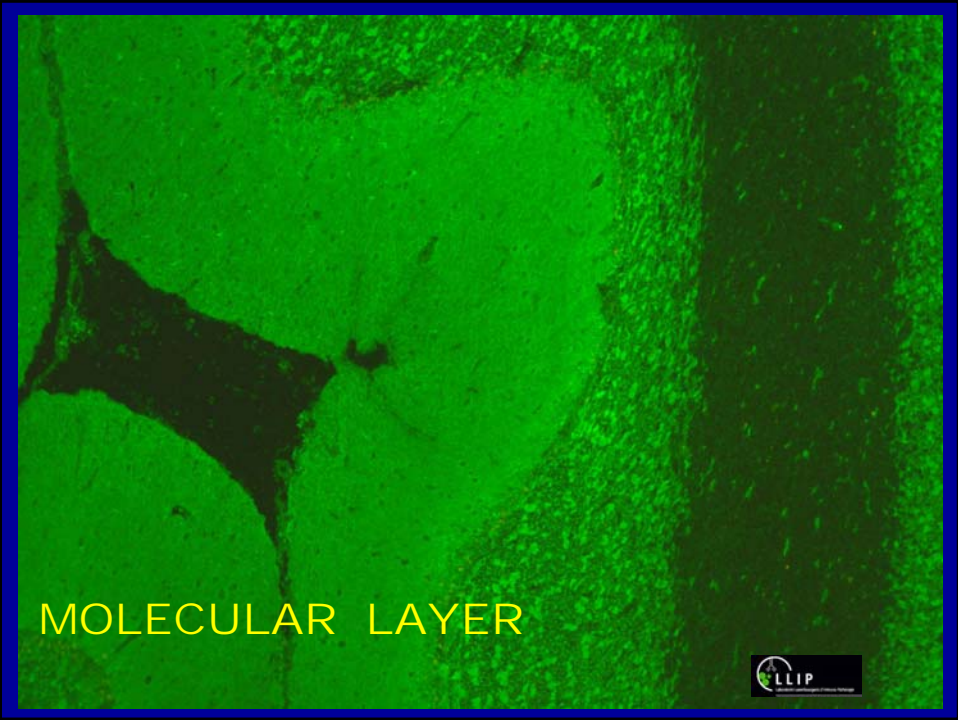
RIA **AChR ,Musk ,VGCC ,VGKC,**

WESTERNBLOT **Cerebellum Extract**



ANTI-NEURONE Hu





**ANTI - NMDAR
TRANSFECTED CELLS**

