



## Developing knowledge

**International Centre for Genetic Engineering and  
Biotechnology**

**A centre of excellence for research and training in genetic engineering  
and biotechnology with regard to the needs of developing world**



# We do it differently

**INTERNATIONAL INSTITUTION** owned by Member Countries

**CUTTING-EDGE RESEARCH BY SCIENTISTS FROM OVER 50 COUNTRIES**

**SCIENTIFIC EXCELLENCE** as a major goal - Research activities supervised by an International Scientific Council that includes two Nobel laureates and top scientists from all over the world

Hands-on **CAPACITY BUILDING** for sharing development - Specific courses held all over the world and long-term training (PhD course + post-doctoral) in the 3 Components

Research focus on **TOPICS OF OUTMOST RELEVANCE FOR DEVELOPING COUNTRIES** (HIV, malaria, tuberculosis and advanced plant biotechnology)

**INTELLECTUAL PROPERTY RIGHTS OWNED AND SHARED** - Research and technology transfer made available to all Member Countries

**Developing knowledge**



**One CENTRE** made of **three** Components, **one** Outstation in Buenos Aires and a Network of **38** Affiliated Centres **in 63** Member States and **83** Signatory Countries

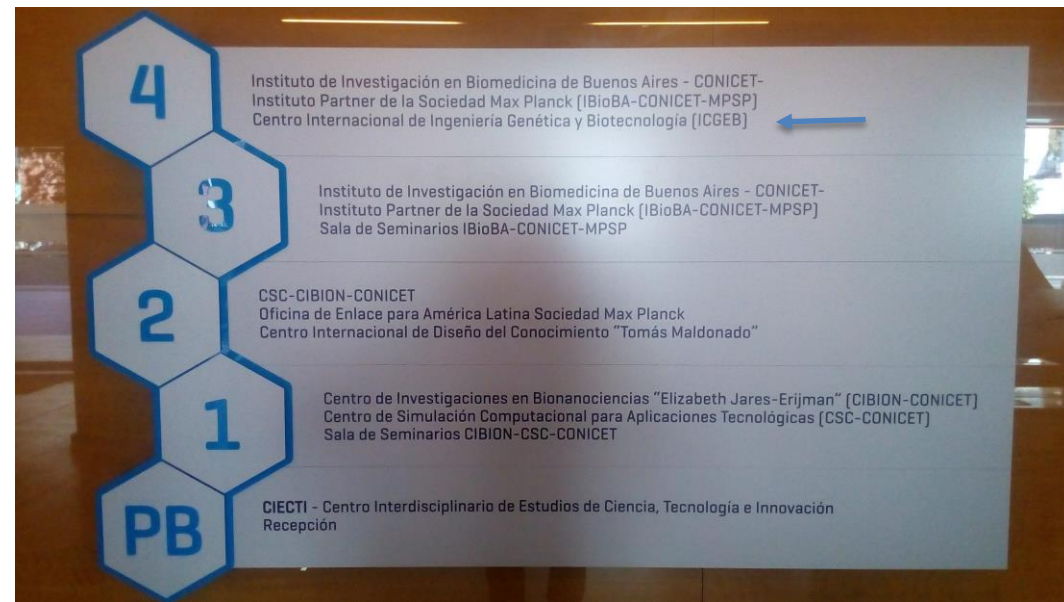
# ICGEB outstation of Buenos Aires



Based in the Science and Technology Polo where MINCyT, CONICET and other scientific Institutes are located



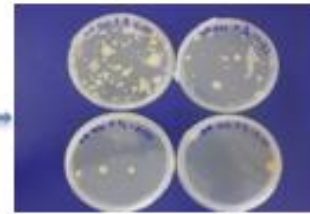
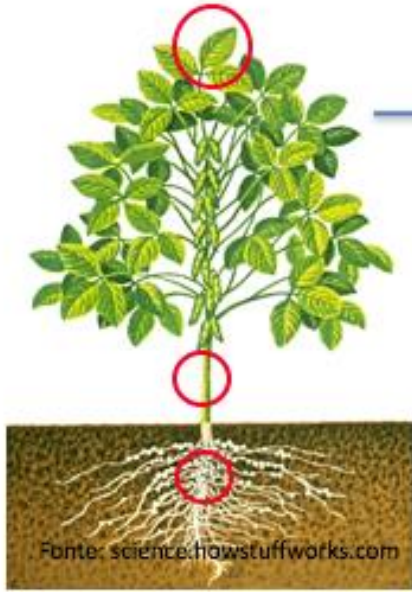
The Polo is a center for the management, production and dissemination of knowledge, nationally and internationally recognized as a relevant center for national academic and scientific development. ICGEB is host of IBioBA, the Institute of Biomedicine of Buenos Aires





# Isolation and characterization of plant growth promoting bacterial endophytes from crops for development of new microbial inoculants

## Isolation



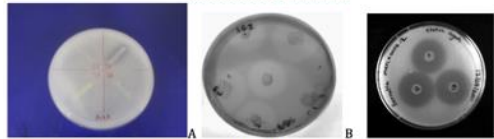
More than 500 strains

## Characterization

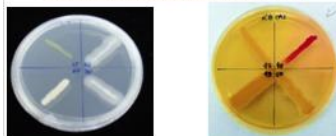
### Endophytic bacteria:

organisms living at least for a period of their life cycle in the interior of a plant without causing negative effects on its development and in some cases contributing to its health and growth.

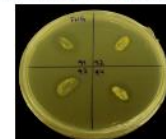
Protease, lipase and chitinase activity  
(extracellular enzymes)



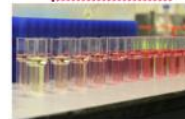
Exopolysaccharides (EPS) and siderophore production



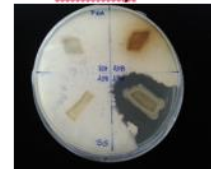
Phosphate solubilization  
(phosphate rock powder)



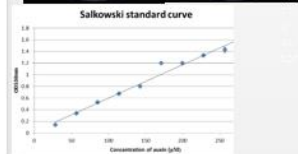
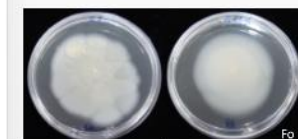
Indolacetic acid (IAA) production



Antimicrobial activity



Swarming and swimming motility



N-fixation and ACC deaminase  
(amplification by PCR)

# PRODUCTION OF BIOGAS FROM IOW

- CONVERSION OF IOW (INDUSTRIAL ORGANIC WASTES) INTO BIOGAS. ADVANTAGES:
  - ENERGY (biogas) PRODUCED FROM WASTE
  - ELIMINATION OF COST OF DISPOSAL
  - FINAL PRODUCT (DIGESTATE) IS A FERTILIZER

EXAMPLE: TISSUE PAPER INDUSTRY

IOW = CELLULOSE WITH SHORT FIBER (NO PAPER)

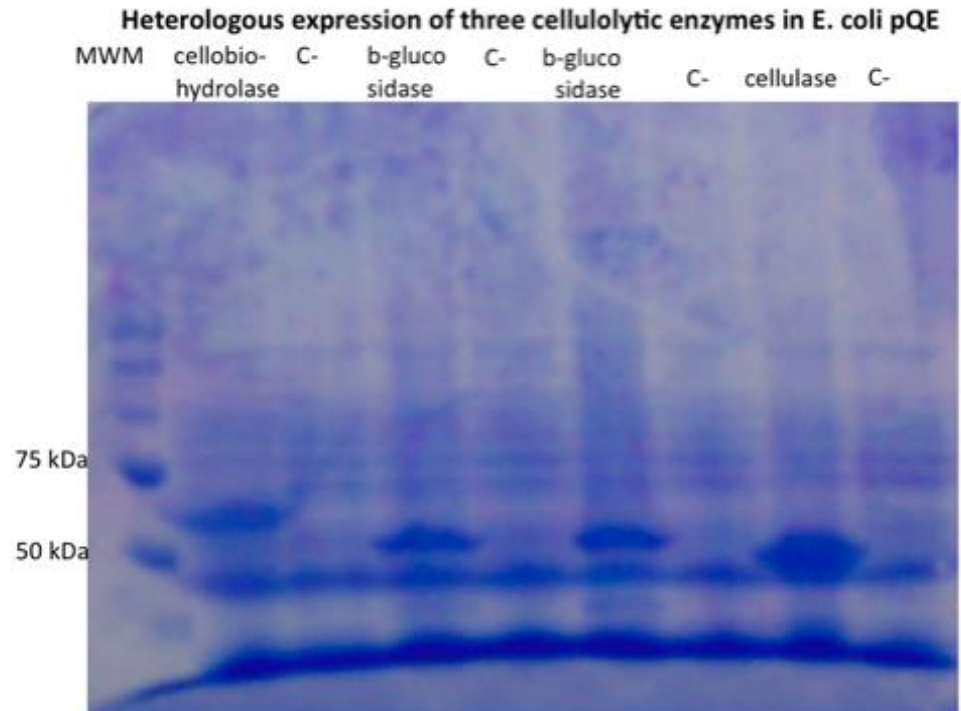
Expression of cellulolytic enzymes  
in *E. coli*:

(i) - endocellulase from *Bacillus pumilus*

(ii) - cellobiohydrolase from  
*Xanthomonas axonopodis* pv  
*glycines*

(iii) - beta-glucosidase from *Bacillus amyloliquefaciens*

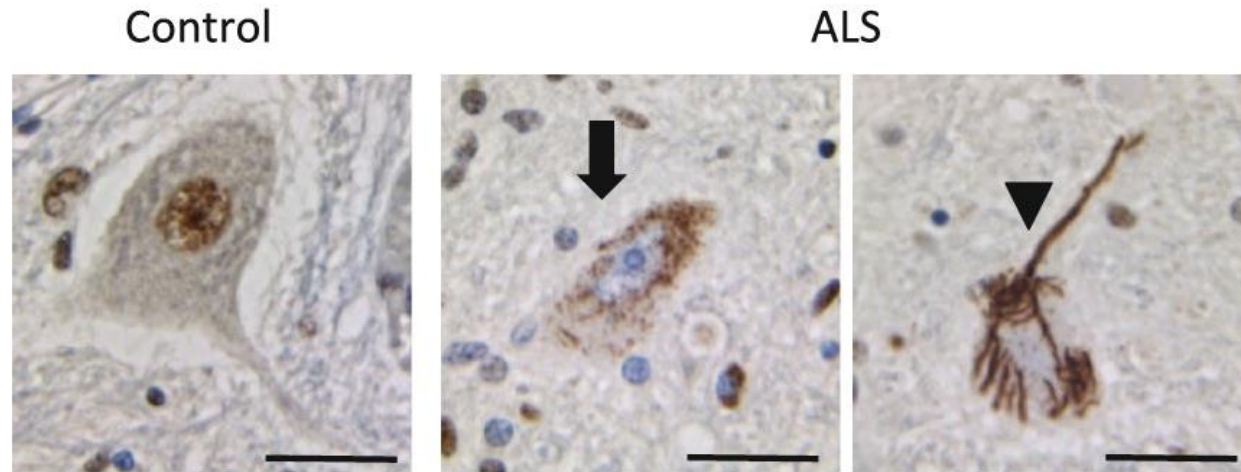
Currently expressing the same  
enzymes in *Pichia pastoris*



**MOLECULAR PATHOLOGY:** The study of the basic mechanism that are involved in the development of disease

**NEURODEGENERATION:** Diseases of generally unknown specific causes and developing during the aging of the organisms

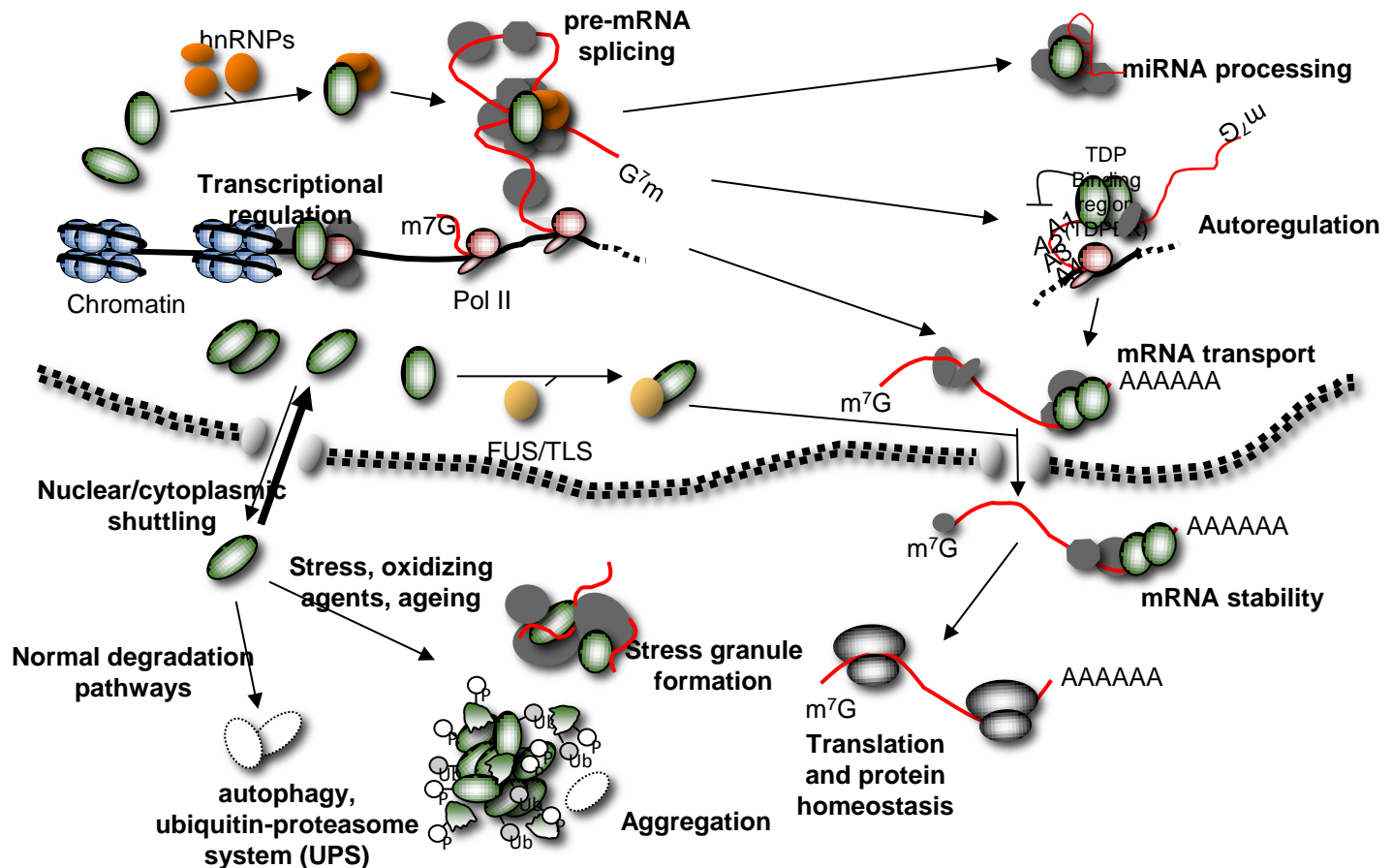
- Amyotrophic lateral sclerosis (ALS) is the most common adult-onset motor neuron disease, and is characterized by the progressive loss of upper and lower motor neurons from the spinal cord, brain stem, and motor cortex, leading to muscle weakness and eventual respiratory failure.
- Approximately 5– 10% of ALS cases are familial with the remaining 90% being sporadic, indicating that both genetic and environmental factors contribute to risk.
- **Despite this diverse etiology of disease, 97 % of patients display a common phenotype in disease affected tissues, namely the deposition of the TAR-DNA binding protein (TDP-43).**



-TDP-43 pathology has also been detected in 40% of Frontotemporal lobar dementia and in 25% to 50% of AD

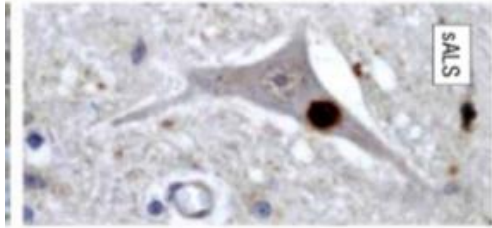


# TAR DNA Binding Protein (TDP 43) is a splicing factor of the hnRNP family that plays a role in many aspects of RNA metabolism.



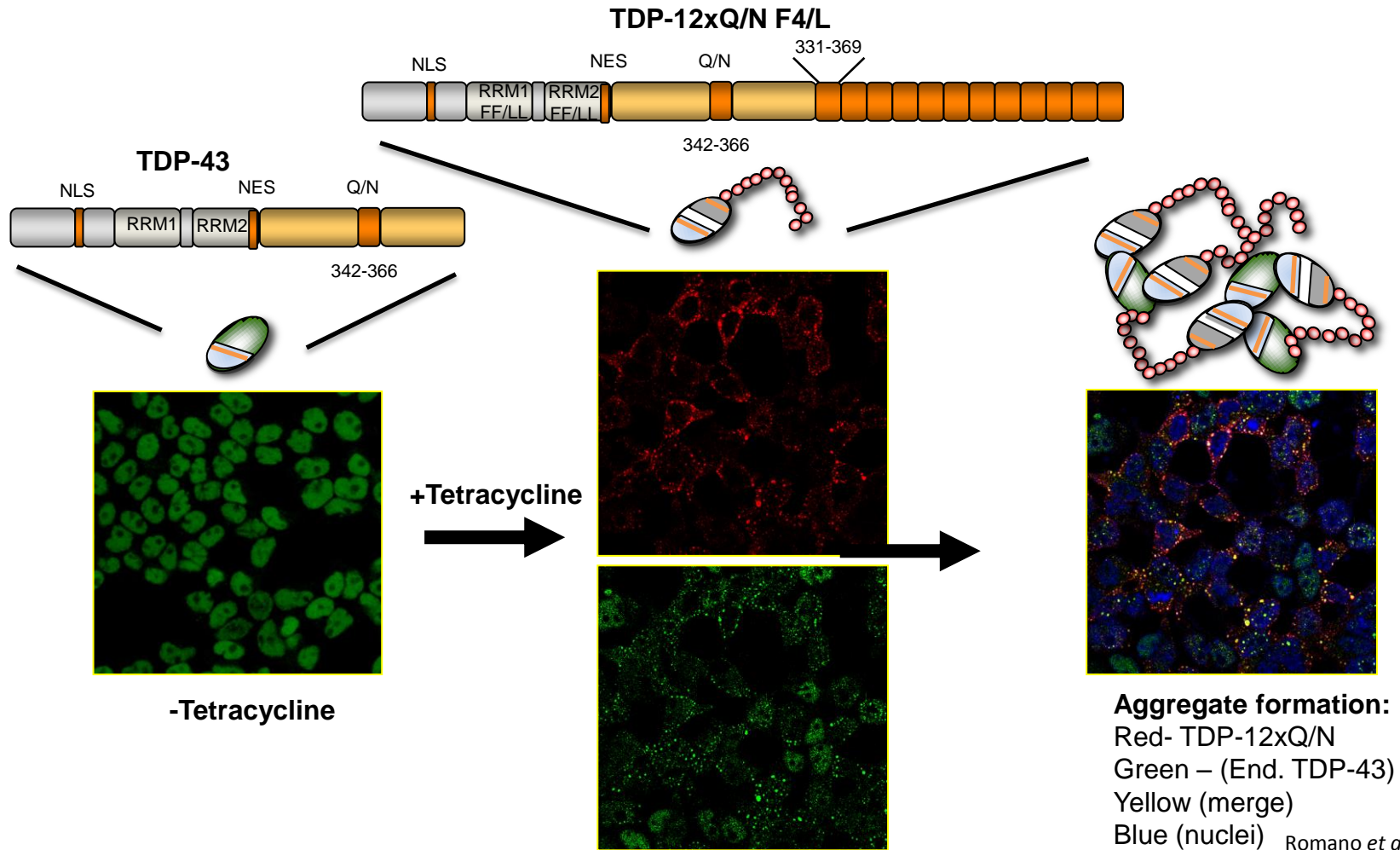
TDP 43 aggregation/dysfunction is central to ALS and FTLD pathogenesis

# Structural determinants TDP-43 aggregation

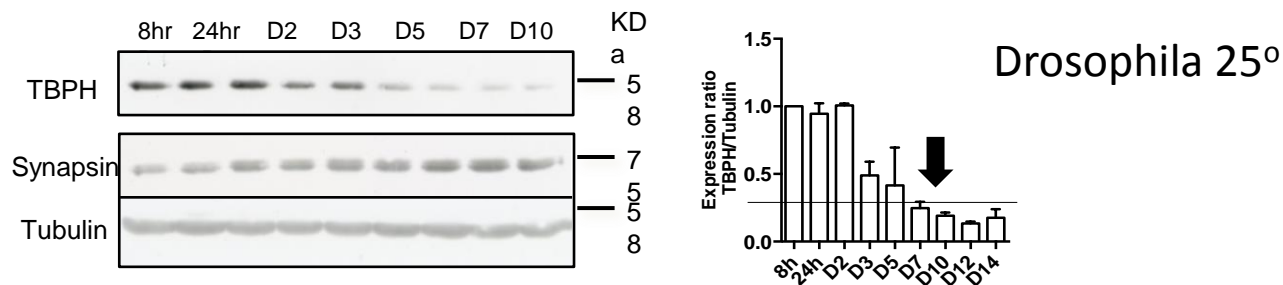


Neumann Science *et al.*, 2006

Ubiquitinated, misfolded and hyper phosphorylated TDP 43 was identified as the major component of the pathological inclusions found in the brain of FTLN and ALS patients. To model the disease it was essential to develop an aggregation model based on non functional TDP 43 fragments

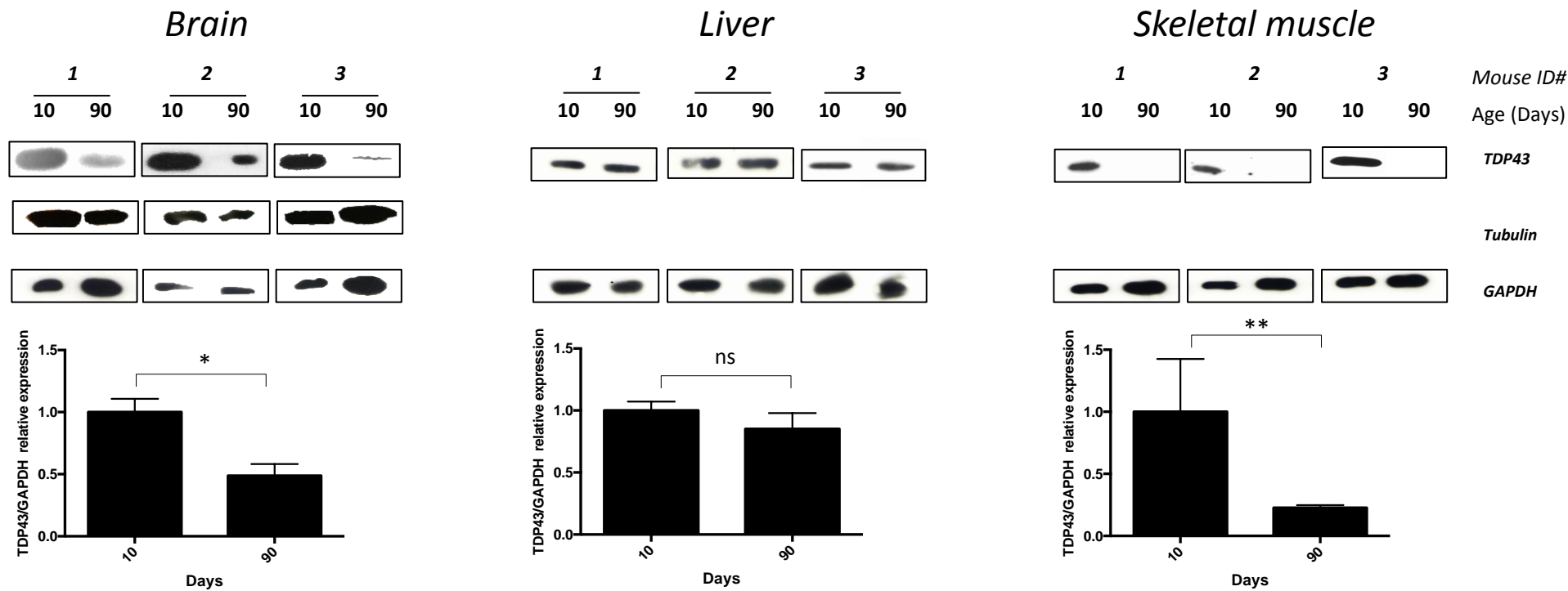


# TDP 43 levels drop during aging, this phenomena correlates with the onset of the locomotion defect in the Drosophila 12xQ/N transgene

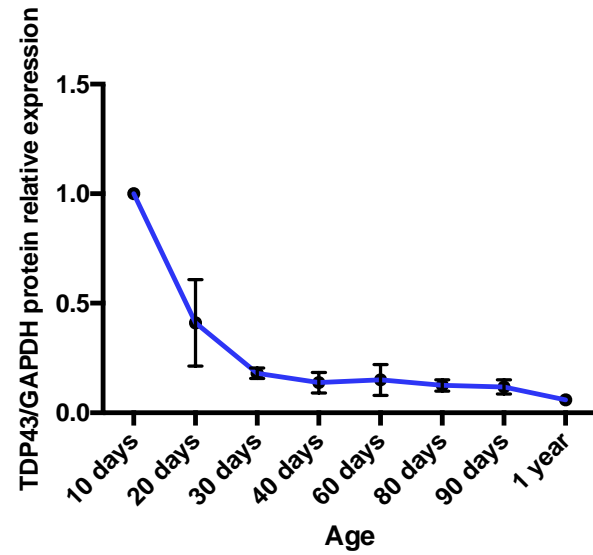


Craganz *et al* Neuroscience 2015

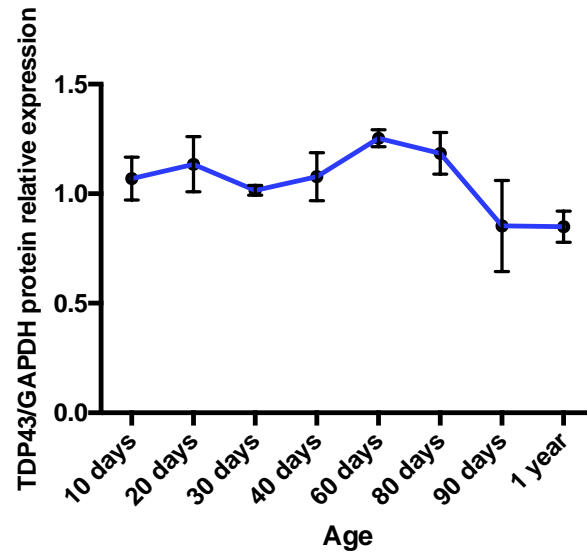
## Reduction of TDP 43 levels with aging in mouse



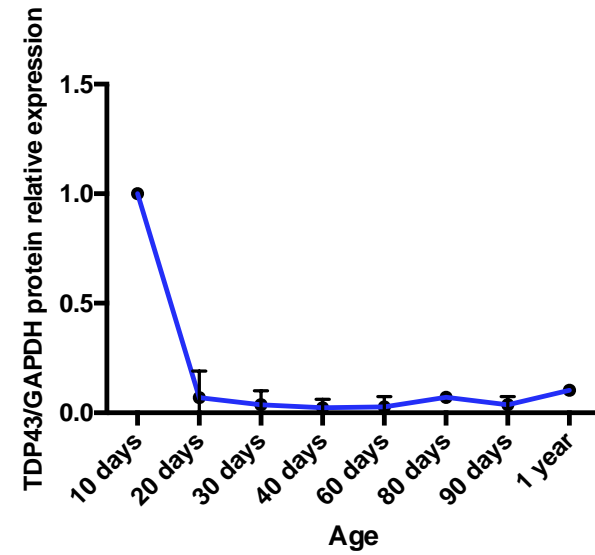
## BRAIN



## LIVER

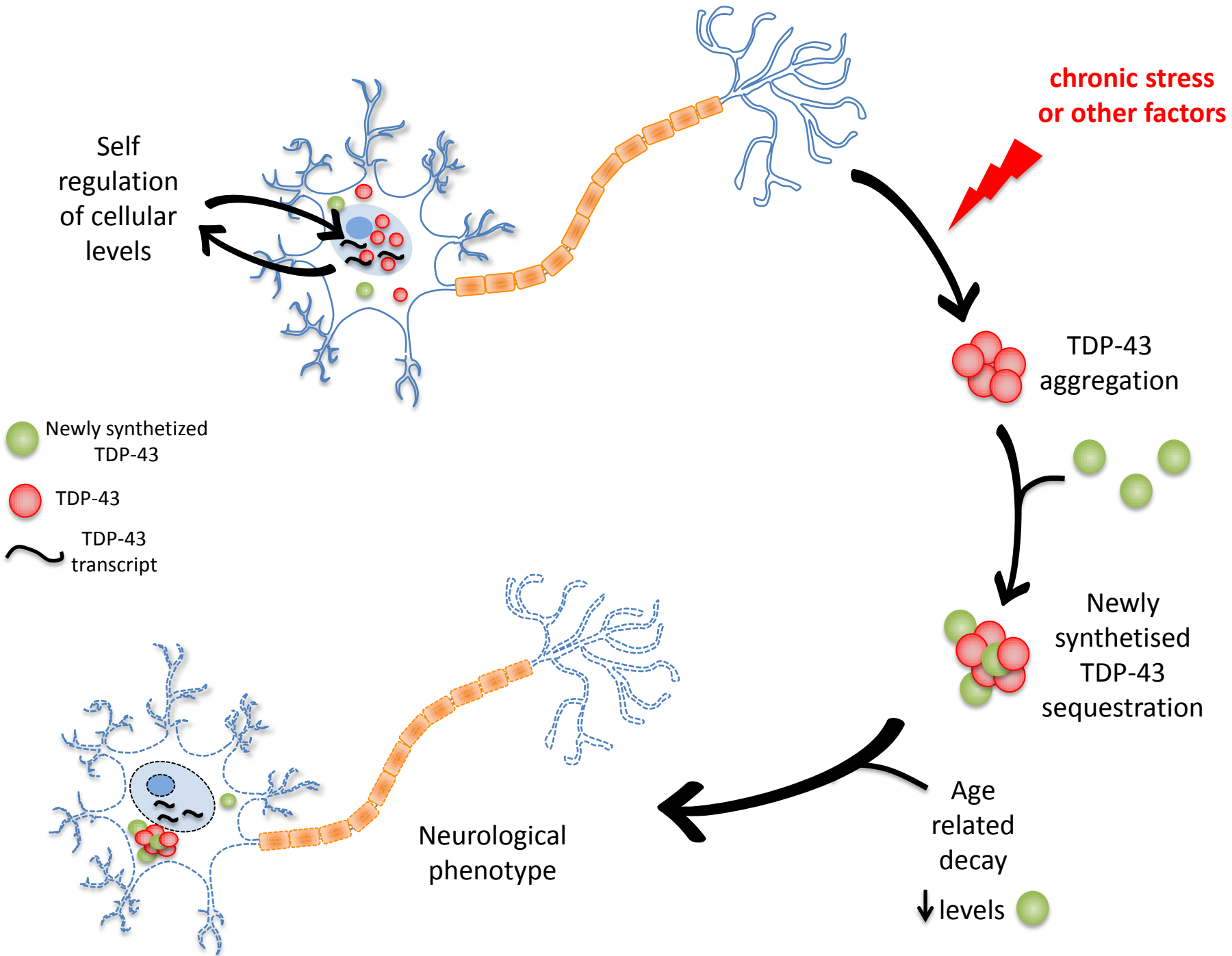


## SKELETAL MUSCLE



TDP 43 cellular levels during aging in mouse tissues





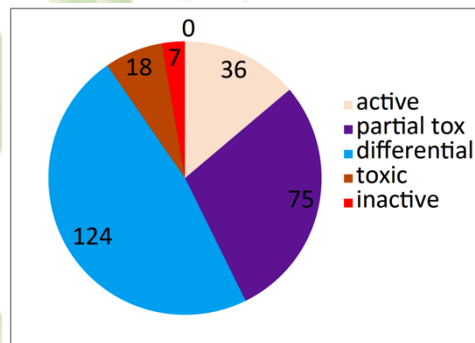
# Screen Cascade and Hit Confirmation Strategy

## FDA set

Pilot Screen. Single shot 1344 cpd  
10uM n=3

5 pts DRC top 532 cpd  
10uM n=2

10 pts DRC  
top 260  
30uM n=2



Reduce aggregates  
by 50% or more

13 classes  
Active, not toxic

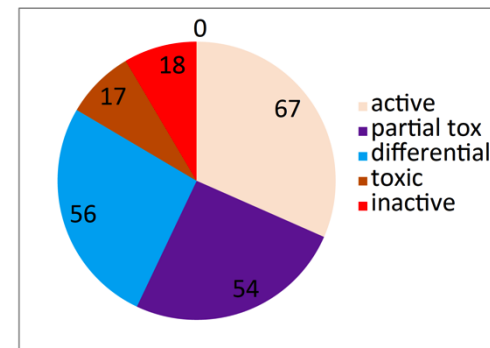
5 classes  
Active, not toxic

## Index set

Pilot Screen. Single shot 10640 cpd  
10uM n=1

5 pts DRC top 611 cpd  
10uM n=2

10 pts DRC  
top 212  
30uM n=2



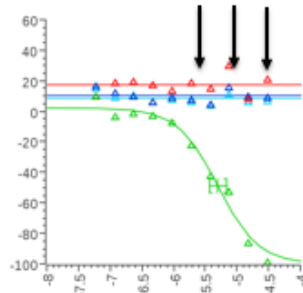
# TDP-43 functional recovery analysis

Drug treatment of the cells in 96 wells plate

↓  
RNA extraction

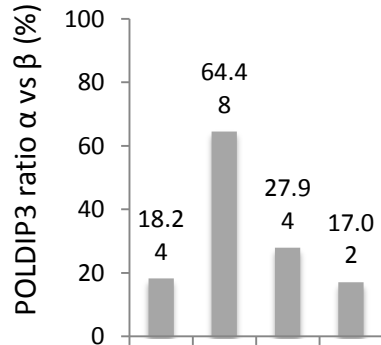
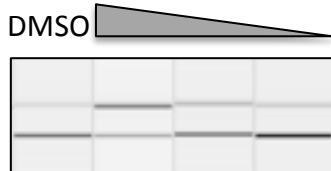
↓  
RT-PCR for POLDIP3 exon 4

↓  
Capillary electrophoresis

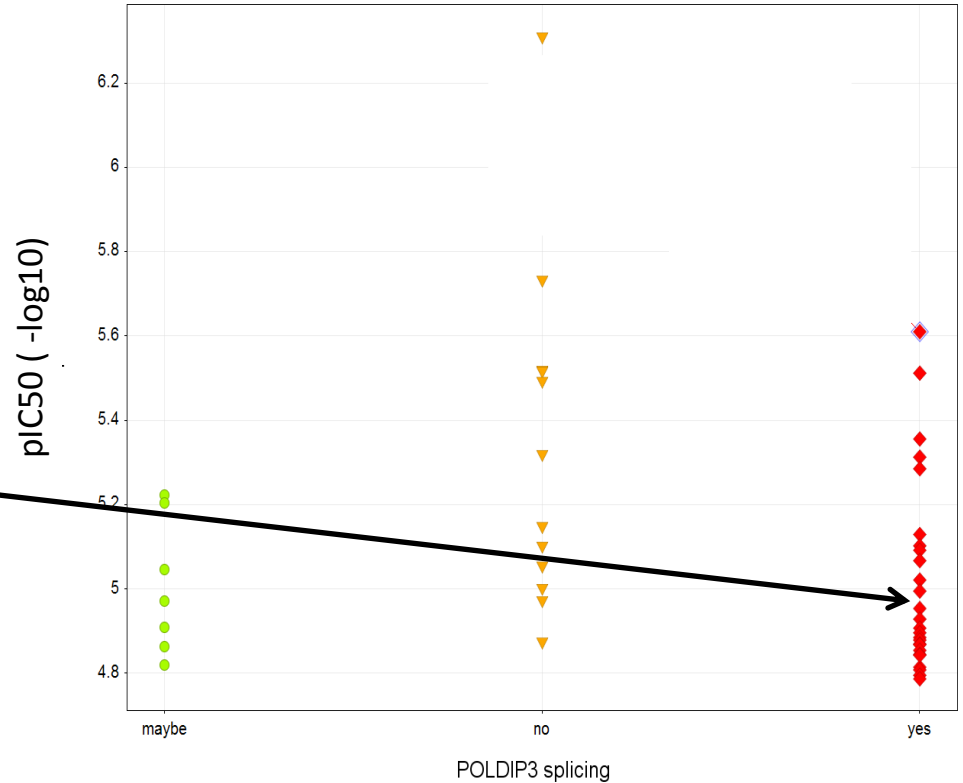


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POLDIP3



Index set

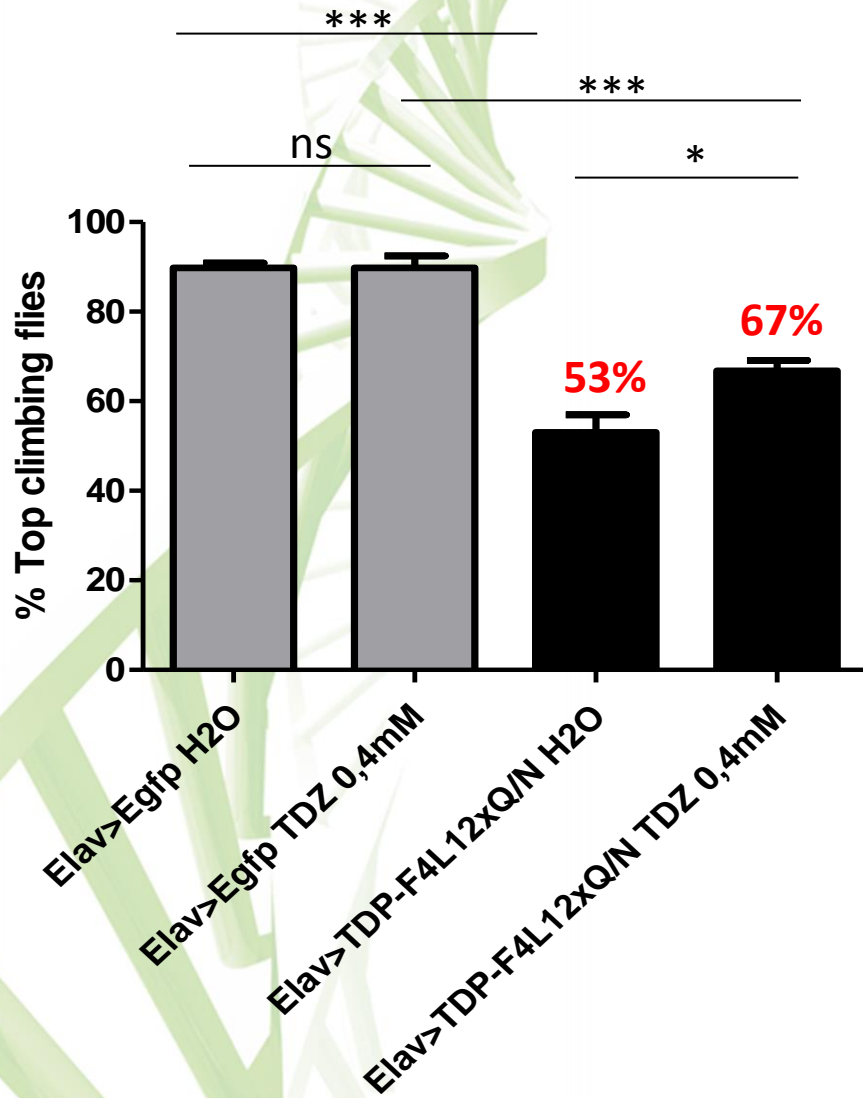


# Pan-neuronal EGFP TDP43 F4L 12Q/N expression day 14





Climbing assay  
Thioridazine 0,4mM Adults



Climbing assay  
Thioridazine 50uM Larvae /0,4mM Adults

