AdipoGen®
LIFE SCIENCES
insights

Progranulin – Marker of Neuroinflammation

Progranulin (PGRN) is a highly conserved secreted cysteine-rich protein that is expressed in multiple cell types, both in the CNS and in peripheral tissues. PGRN is composed of seven ~6kDa granulin (GRN) proteins and acts both directly and via its conversion to granulins, to regulate multifunctional biological activities, including major roles in cancer, inflammation, metabolic disease and neurodegeneration. PGRN is an abundant, non-conventional, stress-induced, extracellular matrix-bound secreted growth factor-like molecule and chaperone. PGRN binds to several functionally different receptor families in a cell/tissue-specific and condition/disease-dependent manner. For example, PGRN binding with TNFR and DR3 has an important anti-inflammatory role in immune cells, particularly Tregs and macrophages. PGRN/Ephrin type-A receptor 2 (EphA2) interaction is involved in the proliferative influence of PGRN. PGRN binds and activates Notch receptors, enhancing the regenerative capacity of injured neurons. PGRN is also a lysosomal resident protein. **Sortilin and lipoprotein receptor- related protein 1 (LRP1) have been demonstrated to be the lysosomal trafficking receptors for PGRN** with the help of Prosaposin. In the brain, PGRN plays a key role in the development, survival, function, and maintenance of neurons and microglia. It regulates lysosomal biogenesis, inflammation, repair, stress response and aging. Absence of progranulin in microglia causes increased production and release of multiple cytokines, suggesting that PGRN regulates microglia activation. PGRN seems to affect microglial proliferation, recruitment, differentiation, activation and phagocytosis, suggesting that PGRN plays a central role in the regulation of neuroinflammatory responses. In neurons, PGRN i) co-localizes in late endosomes and early lysosomes with the transmembrane protein TMEM106B, ii) co-localizes with markers such as BDNF along axons, iii) influences synaptic structure and function at synaptic and extrasynaptic sites, where it is secreted in an activity-dependent manner, and iv) extracellular PGRN is endocytosed and delivered to lysosomes. The lysosomal function of PGRN is not well characterized, but probably involves regulation of proteins such as cathepsins, glucocerebrosidase (GBA) or TMEM106B and likely contributes to neurodegeneration (see Figure). PGRN loss-of-function mutations cause neuronal ceroid lipofuscinosis or frontotemporal Lobar Dementia (FTLD) in a gene dosage-dependent manner and PGRN is therefore **a valuable biomarker of FTLD**. Mutations that reduce PGRN levels also increase the risk for developing Alzheimer's disease, Parkinson's disease and other neurological diseases.

SELECTED REVIEWS: The lysosomal function of progranulin, a guardian against neurodegeneration: D.H. Paushter, et al.; Acta Neuropathol. **136,** 1 (2018) • Progranulin: A conductor of receptors orchestra, a chaperone of lysosomal enzymes and a therapeutic target for multiple diseases: Y. Cui, et al.; Cytokine Growth Factor Rev. **45,** 53 (2019) • Progranulin as a therapeutic target in neurodegenerative diseases: H. Rhinn, et al.; Trends Pharmacol. Sci. **43,** 641 (2022) • Lysosomal functions of progranulin and implications for treatment of frontotemporal dementia: M.J. Simon, et al.; Trends Cell Biol. **(Epub ahead)** (2022)

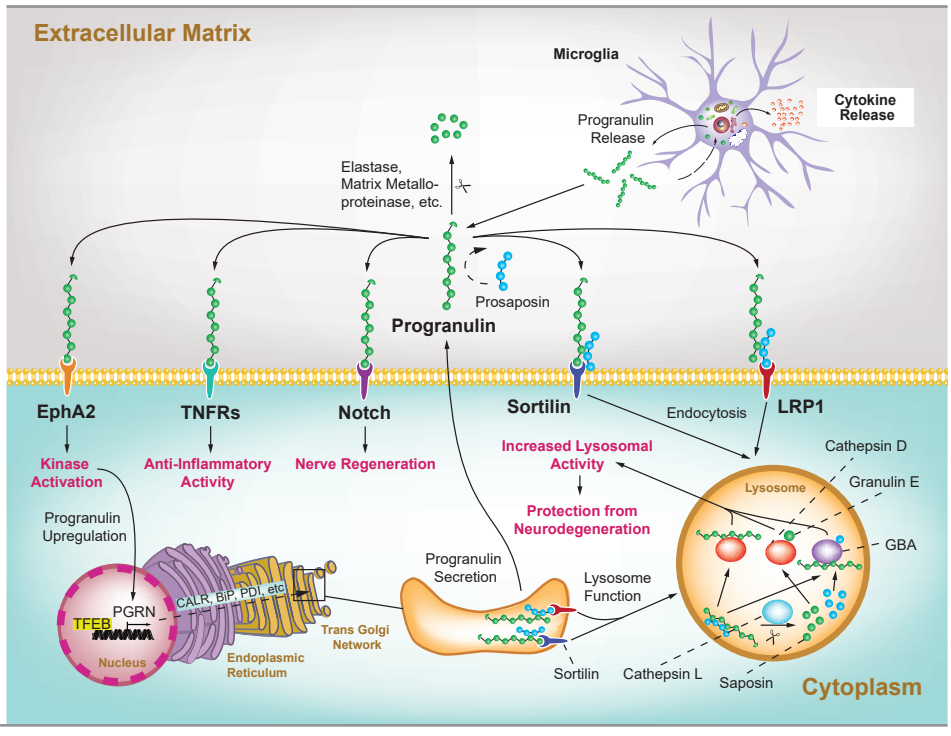


FIGURE: The roles and binding partners of progranulin in neuronal cells.

Visit www.adipogen.com/progranulin-pgrn for a Comprehensive List of Unique Tools!

NEW & Unique Progranulin ELISA Kit Assays

Measuring human *GRN* mutations in Frontotemporal Diseases

GRN mutations are frequent causes of familial frontotemporal lobar degeneration (FTLD). Progranulin expression in plasma predicts *GRN* mutations status, independently of symptom onset proximity. Progranulin loss-of-function mutations are among the most frequent genetic causes, responsible for 20% of familial FTLD. Progranulin levels in plasma or serum, constitute a reliable, cost-effective biomarker, suitable as a screening tool in patients with familial frontotemporal degeneration.

AdipoGen's Progranulin (human) ELISA Kits are the only and unique kits on the market detecting all mutations of Progranulin. They are both validated on Mutated and Null *GRN* plasma samples.

NEW

NEW mAb/mAb-based human Progranulin ELISA Kit

Progranulin (human) ELISA Kit (mAb/mAb)

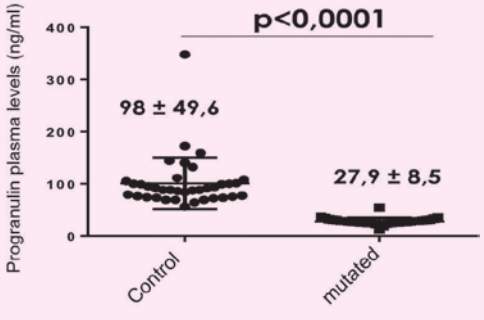
AG-45B-0027 96 wells

Sensitivity: 60 pg/ml
Range: 0.063 ng/ml – 4 ng/ml
Sample: Cell Culture Supernatant, Plasma, Serum
Specificity: Detects human Progranulin.

The new mAb/mAb based human Progranulin ELISA Kit has been thoroughly validated and compared to the standard pAb/pAb based ELISA Kit (Prod. No. AG-45A-0018Y). With this new ELISA Kit, levels below 50 ng/ml are strongly suggestive of *GRN* mutations. In a validation on 191 patient samples, confirmed by a molecular gene analysis, the new kit provided a sensitivity and specificity of 100% for detecting FTLD mutations.

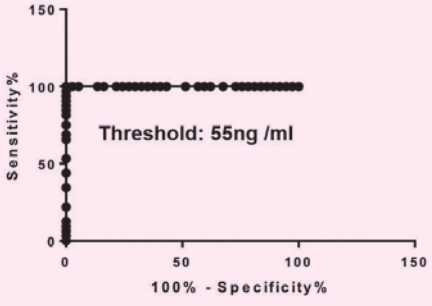
Concentrations of Progranulin plasma levels in FTLD and healthy samples:

Using the new mAb-based ELISA kit (AG-45B-0027), plasma progranulin levels in FTLD-GRN are lower (~28 ng/ml) compared to controls (~98 ng/ml).



ROC curve of the new ELISA Kit:

ROC analysis shows that at a threshold of 55 ng/ml plasma progranulin measured with ELISA Kit (AG-45B-0027) discriminates FTLD-GRN patients from controls with 100% sensitivity and 100% specificity.



AdipoGen® LIFE SCIENCES

APPLICATIONS: **FACS:** Flow Cytometry; **FUNC:** Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry **IP:** Immunoprecipitation; **WB:** Western blot

FORMULATION: **PF** = Preservative free
SPECIES: **Hu** = Human; **Ms** = Mouse; **Rt** = Rat; **Rb** = Rabbit; **Prm** = Primate

The Standard pAb/pAb-based human Progranulin ELISA Kit

Progranulin (human) ELISA Kit

AG-45A-0018YEK	96 wells
AG-45A-0018YTP	2 x 96 wells

Sensitivity: 32 pg/ml
Range: 0.063 ng/ml – 4 ng/ml
Sample: Cell Culture Supernatant, Plasma, Serum, Urine
Specificity: Detects human Progranulin.

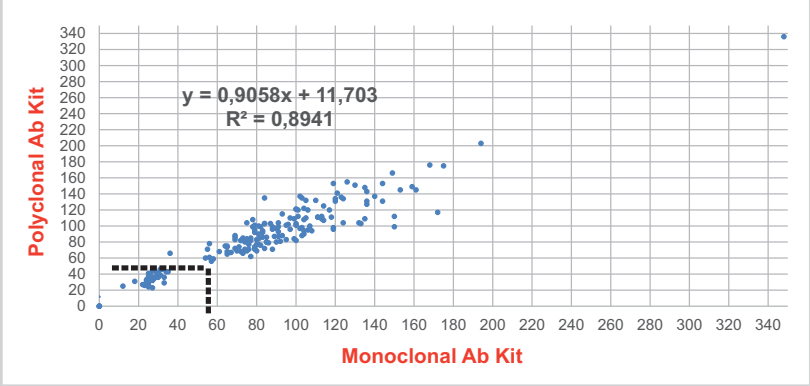
LIT: Plasma progranulin levels for frontotemporal dementia in clinical practice: a 10-year French experience: L. Sellami, et al.; Neurobiol. Aging **91,** 167.e1 (2020)

The Standard pAb/pAb-based human Progranulin ELISA Kit has been widely used by the research community and thoroughly validated on Mutated and Null *GRN* plasma samples.

- ***Trusted Reproducible Results!***
- ***Used to Determine Cut-Off values for FTLD!***
- ***Cited in Hundreds of Scientific Publications!***

Values measured by the AG-45A-0018Y (pAb-based) & AG-45B-0027 (mAb-based) ELISA Kits:

A strong positive correlation was observed between the pAb-based ELISA kit (Reference kit, AG-45A-0018Y) and the newly developed mAb-based ELISA kit (AG-45B-0027) in the measurement of Progranulin plasma levels.



The Standard Mouse & Rat Progranulin ELISA Kits

ASSAYS	PID	SIZE	SAMPLE
Progranulin (mouse) ELISA Kit	AG-45A-0019Y	96 wells | 2 x 96 wells	Cell Culture Supernatant, Serum
Progranulin (rat) ELISA Kit	AG-45A-0043Y	96 wells | 2 x 96 wells	Cell Culture Supernatant, Serum

Progranulin Antibodies & Tagged Proteins

ANTIBODIES	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-Progranulin (human), pAb	AG-25A-0112	100 µg	Guinea pig	ELISA, IHC, WB	Hu
anti-Progranulin (mouse), pAb	AG-25A-0093	100 µg	Rat	ELISA, WB	Ms

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Progranulin (human) (rec.)	AG-40A-0068Y	10 µg | 50 µg	HEK293 Cells	<0.01EU/µg	Hu
Progranulin (rat) (rec.)	AG-40A-0194	10 µg | 50 µg	HEK293 Cells	<0.1EU/µg	Rt

Related Products

ANTIBODY	PID	SIZE	ISOTYPE/SOURCE	APPLICATION	SPECIES
anti-Granulin C (human), pAb	AG-25A-0090	100 µg	Rabbit	ELISA, WB	Hu

PROTEIN	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Granulin C (human) (rec.) (His)	AG-40A-0129	10 µg	E. coli	<1EU/µg	Hu

The Progranulin Receptor Sortilin

The *SORT1* gene is one of the strongest genetic risk factors for Alzheimer's disease and is associated with frontotemporal dementia (FTD). Sortilin controls PGRN trafficking and lysosomal degradation, but PGRN exerts its multiple functions independent of sortilin. Sortilin down-regulation via blocking antibodies, such as Latozinemab Biosimilar, is a key mechanism in increasing PGRN levels suggesting that sortilin is a potential target to correct PGRN reduction, such as that in patients with frontotemporal dementia caused by *GRN* mutations.

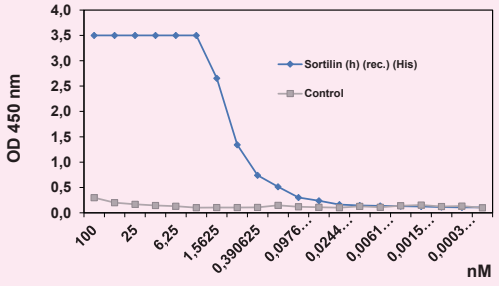
NEW

Sortilin (human) (rec.) (His)

AG-40B-0229 50 µg

Binds to human Progranulin (untagged) (Prod. No. AG-40A-0188Y).

FIGURE: Progranulin (human) (rec.) (untagged) (Prod. No. AG-40A-0188Y) is coated on an ELISA plate at 1 µg/ml overnight at 4°C. Sortilin (human) (rec.) (His) (Prod. No. AG-40B-0229) or a control His-tagged protein (Prod. No. AG-40B-0177) is added (starting at a concentration of 100nM with a twofold serial dilution) during one hour at RT and the interaction is then detected using an anti-His antibody coupled to HRP.

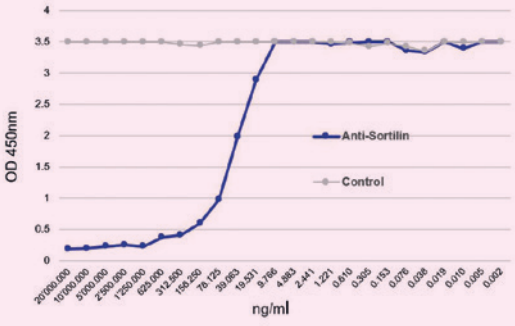


anti-Sortilin (human), mAb (rec.) (blocking) (preservative free) [Latozinemab Biosimilar]

AG-27B-7000PF 100 µg | 500 µg

Clone: Latozinemab
Isotype: Human IgG1κ
Application: Inhibits sortilin binding to progranulin.

FIGURE: Progranulin (human) (rec.) (untagged) is coated on an ELISA plate at 1 µg/ml. Sortilin (human), mAb (rec.) (blocking) [Latozinemab Biosimilar] or an unrelated mAb (Control) is added (starting at a concentration of 20 µg/ml with a twofold serial dilution) together with 250 ng/ml of Sortilin (rec.) (His) for 1 hour. The decreasing ODs observed in the Y axis represent the binding between Progranulin and Sortilin that is inhibited in a dose-dependent manner by Sortilin (human), mAb (rec.) (blocking) [Latozinemab Biosimilar]. This inhibition is not observed with the control antibody.



Unique Tag-free Progranulins

BULK

Progranulin (human) (rec.) (untagged)
AG-40A-0188Y 10 µg | 50 µg

Progranulin (mouse) (rec.) (untagged)
AG-40A-0189Y 10 µg | 50 µg

Progranulin (rat) (rec.) (untagged)
AG-40A-0196Y 10 µg | 50 µg

- *Higher activity compared to tagged Progranulins (binding to Sortilin)*
- *Suitable for in vitro and in vivo studies*
- *Reflects the native sequence with no additional amino acids*
- *Affinity purified*
- *Low endotoxin levels (<0.01EU/µg)*

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