Progranulin [PGRN]

Introduction

Progranulin [1, 2] (PGRN; granulin (precursor); GRN [3-6], epithelin precursor [7, 8]; proepithelin (PEPI) [9]; PC cell-derived growth factor (PCDGF) [10]; acrogranin [11, 12]; paragranulin) is a 593aa cysteine-rich protein of 68.5kDa, that is typically secreted in a highly glycosylated 88kDa form. As a result of proteolytic cleavage of PGRN by extracellular proteases, a family of active 6kDa peptides (granulins (GRNs) A to G and paragranulin) are formed that each contain 10-12 highly conserved cysteine residues. The PGRN gene is widely expressed, particularly in epithelial and hematopoietic cells.

In the periphery, PGRN is implicated in many processes such as tumorigenesis, wound repair and inflammation [13]. Accordingly, PGRN has been reported to be highly expressed in a variety of cancer cell lines and to modulate different aspects of tumorigenesis such as proliferation, invasion and survival [14]. After injury, PGRN is induced in fibroblasts and endothelial cells promoting neo-vascularization [2]. By interacting with the leukocyte protease inhibitor (SLPI) PGRN modulates wound healing [9]. PGRN and GRNs have opposing inflammatory effects. SLPI inhibits the cleavage of PGRN into pro-inflammatory GRNs [9, 15]. PGRN is important for the sexual differentiation of the rat brain [16, 17]. PGRN also promotes neuronal survival and enhance neurite outgrowth in cultured neurons [18]. It has been proposed that PGRN is a stress-response factor in fibroblasts subjected to hypoxia and acidosis [19].

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Progranulin (human) ELISA Kit

- Excellent Quality
- High Sensitivity
- Batch-to-Batch Reproducibility

For Details see Page 3.
PGRN & FTLD

Recent interest regarding PGRN's role in the central nervous system (CNS) was raised after mutations in the PGRN gene, located on chromosome 17, have been identified to cause frontotemporal lobar degeneration (FTLD) [20, 21]. FTLD is a common cause of dementia. The most frequent subtype of FTLD shows ubiquinated-immunoreactive, tau-negative inclusions (FTLD-U) [22, 23]. More recently it was shown that the transactivation of hyperphosphorylated nuclear protein TDP-43 (transactivation response DNA-binding protein 43; TAR DNA-binding protein 43; TARDBP) is the main component of most of these FTLD-U inclusions [24, 25]. The term FTLD-TDP was introduced to specify these FTLD-U inclusions which are TDP-43 positive, what is indeed not always the case [26]. It was further shown that all PGRN mutation carriers have a common FTLD-TDP subtype, referred to as Type 1 [27] or Type 3 [28]. One study provided a possible link between the loss of functional PGRN and TDP-43 pathology, by showing that decreased PGRN levels can induce caspase-dependent accumulation of TDP-43 fragments in vitro [29]. However, this finding was not confirmed by a second study [30].

A total of 66 different loss of function mutations, scattered over all PGRN exons, except exon 13, have been reported. One complete and two partial PGRN deletions have also been identified. An additional 39 patient specific mutations with unknown pathogenic importance were identified in neurodegenerative disease patients. These include 28 missense mutations, 10 silent mutations and one nonsense mutation in PGRN exon 13. Another publication indicated the association of SNPs (single nucleotide polymorphisms) with FTLD-U and enhance neuronal survival; P. Van Damme, et al.; J. Cell Biol. 181, 95 (2009)


PGRN – A Marker?

Interestingly, several studies detected decreased PGRN levels in serum [33], plasma [34, 35] and cerebrospinal fluid (CSF) [35] of PGRN mutation carriers. Therefore PGRN can be considered to be a marker for detecting a PGRN mutation. The measurement of decreased PGRN protein levels in plasma could be a quick and inexpensive test for the presence of a PGRN mutation in a patient [34, 35].

Another study detected serum PGRN concentrations associated to visceral obesity elevated plasma glucose, and dyslipidemia [36]. PGRN might evolve as a novel marker for chronic inflammation in obesity and type-II diabetes (T2D).

LITERATURE REFERENCES:

[1] Progranulin gene expression regulates epithelial cell growth and promotes tumor growth in vivo. Z. He & A. Bateman; Cancer Res. 59, 3222 (1999)
[34] Plasma progranulin levels predict progranulin mutation status in frontotemporal dementia patients and asymptomatic family members: N. Finch, et al.; Brain 132, 583 (2009)
Serum Progranulin Concentrations May Be Associated To Obesity

B.-S. Youn, et al. demonstrated that elevated progranulin serum concentrations are associated with visceral obesity, elevated plasma glucose, and dyslipidemia. They identified progranulin as a novel marker of chronic inflammation in obesity and type-II diabetes (T2D) that closely reflects omental adipose tissue macrophage infiltration. Physical training significantly reduces elevated circulating progranulin in patients with T2D.


Selected Review Articles

- Mutations in progranulin (GRN) within the spectrum of clinical and pathological phenotypes of frontotemporal dementia: J.C. van Swieten & P. Heutink; Lancet Neurol. 7, 965 (2008)
- Recent insights into the molecular genetics of dementia: R. Rademakers & A. Rovelet-Lecrux; TINS Epub ahead of print, (2009)

Progranulin ELISA Kits

Progranulin (human) ELISA Kit
AG-45A-0018EK-KI01 1 x 96 wells
AG-45A-0018TP-KI01 Twin Plex 2 x 96 wells
AG-45A-0018PP-KI01 Penta Plex 5 x 96 wells
Direct measurement of human progranulin in human serum, plasma or cell culture supernatants. SENSITIVITY: 32pg/ml.

Plasma progranulin levels predict progranulin mutation status in frontotemporal dementia patients and asymptomatic family members: N. Finch, et al.; Brain 132, 583 (2009)
Serum Progranulin Concentrations May Be Associated With Macrophage Infiltration Into Omental Adipose Tissue: Y. Byung-Soo, et al.; Diabetes 58, 627 (2009)

Progranulin (mouse) ELISA Kit
AG-45A-0019EK-KI01 1 x 96 wells
AG-45A-0019TP-KI01 Twin Plex 2 x 96 wells
AG-45A-0019PP-KI01 Penta Plex 5 x 96 wells
Direct measurement of mouse progranulin in mouse serum or cell culture supernatants. SENSITIVITY: 60pg/ml.
Progranulin Products

Proteins

Progranulin (human) (rec.)
AG-40A-0068-C010 10 µg
AG-40A-0068-C050 50 µg
Produced in HEK293 cells. Signal peptide and mature progranulin (aa 1-593) is fused at the C-terminus to a FLAG®-tag. PURITY: ≥90% (SDS-PAGE). ENDOOTOXIN CONTENT: <0.1EU/µg protein (LAL-test).

Progranulin (mouse) (rec.)
AG-40A-0080-C010 10 µg
AG-40A-0080-C050 50 µg
Produced in HEK293 cells. Signal peptide and mature mouse progranulin (aa 1-589) is fused at the C-terminus to a FLAG®-tag. PURITY: ≥90% (SDS-PAGE). ENDOOTOXIN CONTENT: <0.1EU/µg protein (LAL-test).

Granulin C
Granulin C (human) (rec.) (His)
AG-40A-0129-C010 10 µg
AG-40A-0129-C050 50 µg
Produced in E. coli. The mature peptide of human granulin C (aa 364-430) is fused at the C-terminus to a His-tag.

Progranulin (human) (rec.) (His)
AG-40A-0129-C010 10 µg
AG-40A-0129-C050 50 µg
Produced in E. coli. The mature peptide of human progranulin (aa 1-593) is fused at the C-terminus to a His-tag.

Antibodies

new  anti-Progranulin (human), mAb (PG359-7)
AG-20A-0052-C100
100 µg
CLONE: PG359-7. ISOTYPE: Mouse IgG1. IMMUNOGEN: Recombinant human progranulin. SPECIFICITY: Recognizes human progranulin. Detects a band of ~90kDa by Western blot. APPLICATION: IHC, IP, WB.

new  anti-Progranulin (mouse), mAb (PG319-1)
AG-20A-0077-C050
50 µg
AG-20A-0077-C100
100 µg
CLONE: PG319-1. ISOTYPE: Rat IgG2. IMMUNOGEN: Recombinant mouse progranulin. SPECIFICITY: Recognizes mouse progranulin. Detects a band of ~90kDa by Western blot. APPLICATION: WB.

anti-Progranulin (mouse), pAb
AG-25A-0093-C100
100 µg
From rat. IMMUNOGEN: Recombinant mouse progranulin. SPECIFICITY: Recognizes mouse progranulin. Weakly cross-reacts with human progranulin. Detects a band of ~90kDa by Western blot. APPLICATION: WB.

anti-Progranulin (mouse), pAb
AG-25A-0090-C100
100 µg
From rabbit. IMMUNOGEN: Recombinant human granulin C. SPECIFICITY: Reacts with human granulin C and human progranulin. APPLICATION: WB.

FIGURE 1: The effects of phospho-ERK1/2 and non-phospho-ERK1/2 by progranulin (human) (rec.) (Prod. No. AG-40A-0068) in THP-1 cells.

Method: To examine the signal of phospho-p44/42 MAP kinase, reactions were carried out at 37°C over 0, 30, 60 min., respectively by adding the recombinant protein (100ng/ml) to the THP-1 monocyte cells, which were maintained with serum starvation for 24 hours. Recombinant proteins in lanes 1, 2 and 3 were subjected to THP-1 monocyte cell treatments over 0, 30, 60 min., respectively.


Method: To examine the signal of phospho-p44/42 MAP kinase, reactions were carried out at 37°C over 0, 30, 60 min., respectively by adding the recombinant protein (500ng/ml) to the MCF10A human breast epithelial cells, which were maintained with serum starvation for 24 hours. Recombinant proteins in lanes 1, 2, 3 and 4 were subjected to MCF10A human breast epithelial cell treatments over 0, 30, 60 min., respectively.

Progranulin Products

Progranulin (human) (rec.)
AG-40A-0068-C010 10 µg
AG-40A-0068-C050 50 µg
Produced in HEK293 cells. Signal peptide and mature human progranulin (aa 1-593) is fused at the C-terminus to a FLAG®-tag. PURITY: ≥90% (SDS-PAGE). ENDOOTOXIN CONTENT: <0.1EU/µg protein (LAL-test).

Progranulin (mouse) (rec.)
AG-40A-0080-C010 10 µg
AG-40A-0080-C050 50 µg
Produced in HEK293 cells. Signal peptide and mature mouse progranulin (aa 1-589) is fused at the C-terminus to a FLAG®-tag. PURITY: ≥90% (SDS-PAGE). ENDOOTOXIN CONTENT: <0.1EU/µg protein (LAL-test).