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Bridging Knowledge and the Economy

PCSK9 inhibitors cell-based screening assay

Reference: VAL-503-IRCM

Keywords: cholesterol, lipid, PCSK9, convertase inhibitors, LDLR, hypocholesterolemic agents, cardiovascular disease

Background

The Proprotein Convertases (PCs) are responsible for the limited proteolysis of multiple polypeptide precursors, generating a large diversity of bioactive molecules in the organism. Furthermore, PCs are involved in a large variety of biological processes and were shown to be implicated in several human diseases.

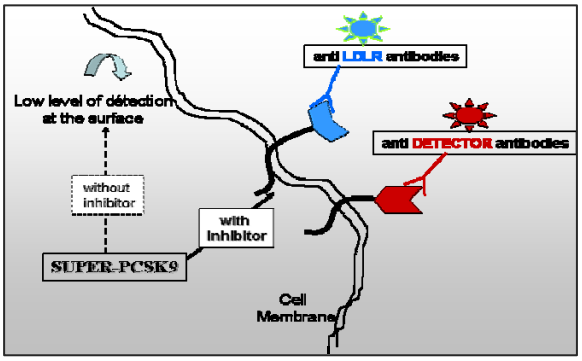
Some PCs, such as SKI-1 and PCSK9, play critical roles in the regulation of lipid metabolism and cholesterol homeostasis, either through activation of specific membrane-bound transcription factors (e.g. SREBP-1 and -2 by SKI-1), or through a reduction at the cell surface of the low density lipoprotein receptor (LDLR) and the subsequent increase in the circulating blood stream LDL-cholesterol- resulting from the PCSK9 activity. For instance, point mutations in the PCSK9 gene are associated either with hypo or hypercholesterolemia and the complete knockout of PCSK9 in mice showed a ~50% reduction in circulating blood stream LDL-cholesterol.

Technology

The technology consists in a positive sensitive cell-based screening assay, selective for cellular PCSK9 activities. In this assay, the cell line harbors detectors, a very low to undetectable level of different cell surface receptors, the absence of which depends upon activity of the SUPER-PCSK9. The presence of PCSK9 inhibitors is detected by the reappearance of these detectors.

Applications

Since PCSK9 is a validated target for lipid metabolism, this technology will allow the detection of a new class of drugs for reduction of circulating blood stream LDL-cholesterol.



Competitive Advantages

- Adaptable for high throughput screening.
- Positive and sensitive screening assays allowing for rapid identification of clinically relevant inhibitors of PCSK9 activities.
- Possibility of using several independent detectors.
- Cell-based assay selecting against toxic compounds for cells.
- New class of drugs could be used as a stand alone therapy or in combination with existing ones (Statins or Ezetimibe)

Patent Status

Patent application pending in CA, US and EU (Q2/2007)

Business Opportunity

Univalor is seeking licensing agreement with a commercial partner.

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