

Biochemistry

Inhibitory role of GRK2 on insulin-induced glucose transport

The evidence of crosstalk between the actions of G protein-coupled receptors (GPCRs) and receptor tyrosine kinases (RTKs) has been widely described. However, recent studies have shown that this interaction occurs not only at the receptor level, but it can also encompass components of both signaling pathways. Exciting work from Jerrold Olefsky's group has described the participation of G protein-coupled receptor kinase 2 (GRK2) – an important protein that has a key role in desensitization of GPCRs – in the negative regulation of insulin-induced glucose transport [4].

The group previously reported that the heterotrimeric G protein α -subunit, G α /11 can mediate insulin-stimulated glucose

transport [5]. GRK2 contains a regulator of G protein signaling (RGS) domain with specificity for G α /11, therefore, they decided to analyze the role of GRK2 in the inhibition of G α /11 function using three mutants of GRK2: the GRK2 wild type, a kinase deficient mutant of GRK2 and a mutant without the RGS domain [4].

They demonstrated that the GRK2 wild type and the kinase-deficient GRK2 mutant inhibited the insulin-mediated GLUT4 translocation. Interestingly, the mutant GRK2 lacking the RGS domain had no effect, suggesting that GRK2 functions, through its RGS domain, as an endogenous inhibitor of insulin-induced glucose transport, by interfering with G α /11 signaling.

Moreover, inhibition of GRK2 by antibody microinjection, dominant-negative GRK2 expression, or siRNA-mediated GRK2

knockdown, all increased insulin sensitivity for stimulation of glucose transport. Thus, these results suggest that GRK2 has a new role as an endogenous protein inhibitor of the insulin-induced glucose transport, and can also be an important target for antidiabetic therapeutics acting as insulin sensitizer.

- 4 Usui, I. *et al.* (2004) GRK2 is an endogenous protein inhibitor of the insulin signaling pathway for glucose transport stimulation. *EMBO J.* 23, 2821–2829
- 5 Imamura, T. (1999) G α -q/11 protein plays a key role in insulin-induced glucose transport in 3T3-L1 adipocytes. *Mol. Cell. Biol.* 19, 6765–6774

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Business

Collaborations

Phenomix signs major discovery collaboration with Genentech

Phenomix Corporation (<http://www.phenomixcorp.com>), have announced a collaboration with Genentech (<http://www.gene.com>) to identify and prioritize drug targets for the treatment of immune disorders.

Phenomix will also receive research funding and future payments on products emerging from the collaboration that are developed and commercialized by Genentech. In exchange, Genentech will obtain exclusive rights to research, develop, manufacture and commercialize potential therapeutics.

Laura Shawver, President and CEO of Phenomix, said: 'Our forward genetics approach differs fundamentally from genomics era attempts at novel target discovery... This partnership of our unique technology and Genentech's disease

expertise presents a fantastic opportunity to identify novel intervention points and develop new treatments for debilitating diseases.'

'Forward genetics has been extremely productive in identifying critical genes in lower organisms such as drosophila and nematodes,' said Chris Goodnow, Founder and Chief Scientific Officer of Phenomix. 'We're excited to be collaborating with Genentech, given their leadership in immune-related research, development and commercialization.'

Abbott and Celera announce cancer therapeutics collaboration

Abbott Laboratories (<http://www.abbott.com>) and Celera Genomics Group (<http://www.celera.com>) have announced the formation of a strategic collaboration to discover, develop and commercialize therapies for the treatment of cancer.

The collaboration will encompass the development of therapeutic antibodies and small-molecule drugs against over-expressed cell-surface proteins that have been associated with cancer and validated as therapeutic targets through proteomics research at Celera.

This collaboration pairs Celera's proteomics and target discovery efforts with Abbott's drug research, development, manufacturing and commercialization expertise. Abbott brings a full range of research capabilities and specific technology platforms, including expertise in RNAi for target validation, discovery of therapeutic small molecules and antibodies, and preclinical and clinical development.

'This collaboration is another important strategic step in Abbott's oncology research program,' said Jeffrey M. Leiden, President and COO,

Pharmaceutical Products Group at Abbott. 'By combining Celera's leading-edge capabilities in proteomics and target discovery with Abbott's expertise in both small molecules and biologics, we believe that we will be able to deliver effective new therapies for the patients fighting certain cancers.'

Kathy Ordoñez, President of Celera Genomics, said: 'This collaboration demonstrates the potential value of Celera's therapeutic targets and technology to industry leaders such as Abbott. It represents an important milestone toward our goal of developing a pipeline of targeted therapies to address unmet medical needs in oncology.'

Vakzine Projekt Management and Probiogen collaboration

Vakzine Projekt Management GmbH (VPM; <http://www.vakzine-manager.de>) and Gesellschaft für Biotechnologische Forschung GmbH (GBF; <http://www.gbf.de>) and ProBioGen AG (<http://www.probiogen.de>), have entered a collaboration agreement on the process development and manufacturing of VPM's Soluferon®, a novel interferon-β molecule to be developed for the treatment of multiple sclerosis.

'This collaboration with VPM underpins our ability to provide innovative, economical and easily up-scalable manufacturing processes in the highly competitive arena of biopharmaceutical manufacturing,' said Michael Schlenk, CEO of ProBioGen. 'It has been a highly rewarding experience to have found a partner who is similar to our organisation in the ability to combine innovation with flexibility, pragmatism and dedication' said Albrecht Läufer, CEO of VPM.

ProBioGen, a German biotechnology company founded 1994 as a spin-off from the university hospital Charité in Berlin, offers services in the research and production for pharmaceutical and biotechnology companies. VPM organizes preclinical and clinical development of vaccines and related immunologically active substances and acts under a contract with GBF (the German Research Centre for Biotechnology).

Business was written by
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People

Appointments

James A. Cour appointed President and CEO of Aastrom

Aastrom Biosciences (<http://www.aastrom.com>), a developer of proprietary stem cell-based products for the regenerative repair of damaged human tissues, have appointed James A. Cour as President and Chief Operating Officer.

R. Douglas Armstrong, the company's Chairman and CEO, commented: 'Cour's operational and business development capabilities will be of tremendous value to Aastrom, and will help the Company continue to meet its goals.' Cour previously held executive level management positions with several companies, including Baxter International, Windsor VanGelder and Cytomedix, and brings to Aastrom over 20 years of business success and accomplishments, ranging from expertise in operations and business development to strategic planning and international business.

'I am very excited to be joining Aastrom,' said Cour. 'The Company is making strong progress toward its goal of bringing its bone marrow stem cell products to standard medical practice, and I welcome the opportunity to actively participate in the achievement of that goal.'

Adolor Corporation appoints James E. Barrett as CSO

James E. Barrett has been appointed Chief Scientific Officer of Adolor Corporation (<http://www.adolor.com>), which specializes in the discovery, development and commercialization of prescription pain-management products. Barrett will also serve as President, Research, and will report to David Jackson, Senior Vice President, R&D.

'Jim brings Adolor a wealth of experience in neuropharmacology research and development and a proven track record in the development of product portfolios,' stated Jackson. 'I look forward to working with him in our efforts to continue the progress in the development of our lead product,

Entereg™ (alvimopan), as well as to expand our pipeline of novel pain management products.'

Barrett has over 20 years of pharmaceutical industry and academic research experience. Most recently, he served as President, R&D at Memory Pharmaceuticals, where he oversaw all exploratory, discovery, preclinical and clinical research and development activities for the company. He was also recently elected President of the American Society for Pharmacology and Experimental Therapeutics for the 2005 term.

PPD names Colin Shannon Executive VP of Global Clinical Operations

Pharmaceutical Product Development (PPD; <http://www.ppd.com>) have appointed Colin Shannon to the newly created position of Executive VP of Global Clinical Operations. In this role, Shannon will oversee clinical, biostatistics and data management operations worldwide.

Shannon joined PPD in 1995 and has served for the past four years as COO for the company's European operations. Previous roles with the company included Executive Director and Chief Financial Officer for Europe. 'Under Colin's leadership, PPD operations in Europe experienced improved efficiencies and significant growth, and we are confident he will continue to demonstrate his ability to achieve quality performance and outstanding success in his new role directing our global operations,' said Fred Davenport, President of PPD.

As a leading global provider of discovery and development services and products for pharmaceutical, biotechnology and medical device companies, PPD applies innovative technologies, therapeutic expertise and a commitment to quality to help clients maximize the return on their R&D investments.

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