molecular interventions
pharmacological perspectives from biology, chemistry and genomics

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DEPARTMENTS

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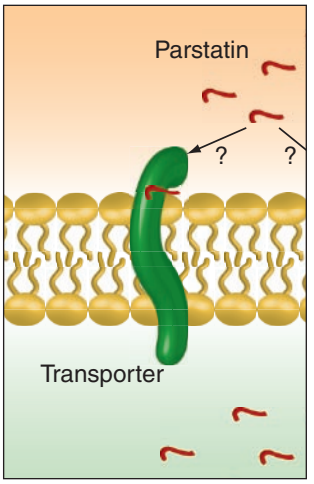

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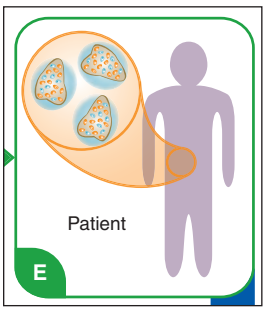
Regulating the regulator: Keeping PAR1's pro-angiogenic activity in check?

VIEWPOINTS

Angiogenesis, the process of forming new blood vessels, is a well established and clinically relevant feature of a variety of disease states. Whether blood vessels sprout in a given tissue environment depends on the balance between factors that stimulate angiogenesis and those that impede it. Potent pro-angiogenic factors such as vascular endothelial growth factor (VEGF) have been identified, validated, and successfully used in the clinic. Likewise, anti-angiogenic factors are also emerging as biologically relevant and therapeutically useful entities. PAR1 is a G protein–coupled receptor (GPCR) that participates in hemostasis and vascular development and that mediates the angiogenic activity of thrombin. PAR1 is activated through proteolytic cleavage of its first forty-one extracellular residues by a variety of proteases, most notably thrombin. However, little effort has focused on the forty-one–residue peptide fragment liberated during PAR1 activation. Tsopanoglou and colleagues have now demonstrated that this peptide, parstatin, has intriguing anti-angiogenic activity, and, in a follow-up study, they demonstrate its potential pharmacological utility using a rat model of ischemic heart disease.

Michael B. Duncan and Raghu Kalluri

Regenerative medicine utilizes cutting-edge technologies to repair and replace damaged cells, tissues, and organs for functional restoration. This broadly interdisciplinary field draws from cell and molecular biology, genetics, immunology, surgical sciences, physiology, biomedical and tissue engineering, chemical and material sciences, and nanotechnology. Certainly, pharmacology serves as an integral component of regenerative medicine, a concept first elucidated in depth in this journal. We operationally define regenerative pharmacology as the application of pharmacological sciences to accelerate, optimize, or characterize the development, maturation, and function of bioengineered and regenerating tissues, either in vitro or in vivo. Diabetes mellitus, a condition defined by elevated levels of glucose in the blood, represents a compelling target for regenerative medicine, through a variety of complementary strategies. A recent report from the laboratory of Peter Schultz of small molecules capable of stimulating the proliferation of insulin-producing pancreatic β cells highlights the potential of regenerative pharmacology to develop novel treatments for this important disease.



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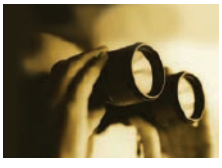
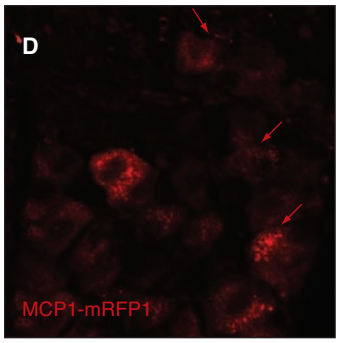
Proliferating β cells: Big things from small molecules

Mark E. Furth and George J. Christ



REVIEWS



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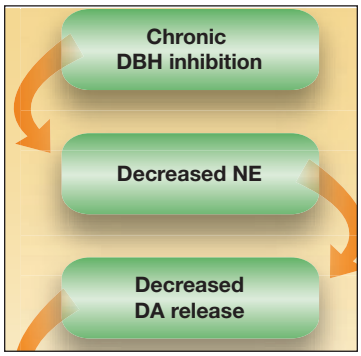
G protein–coupled pain



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Inhibiting addiction