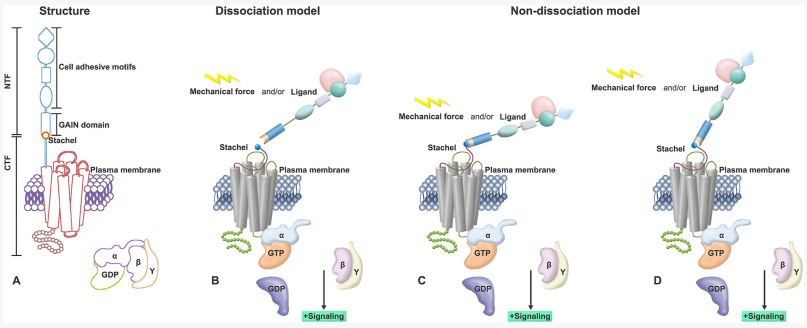
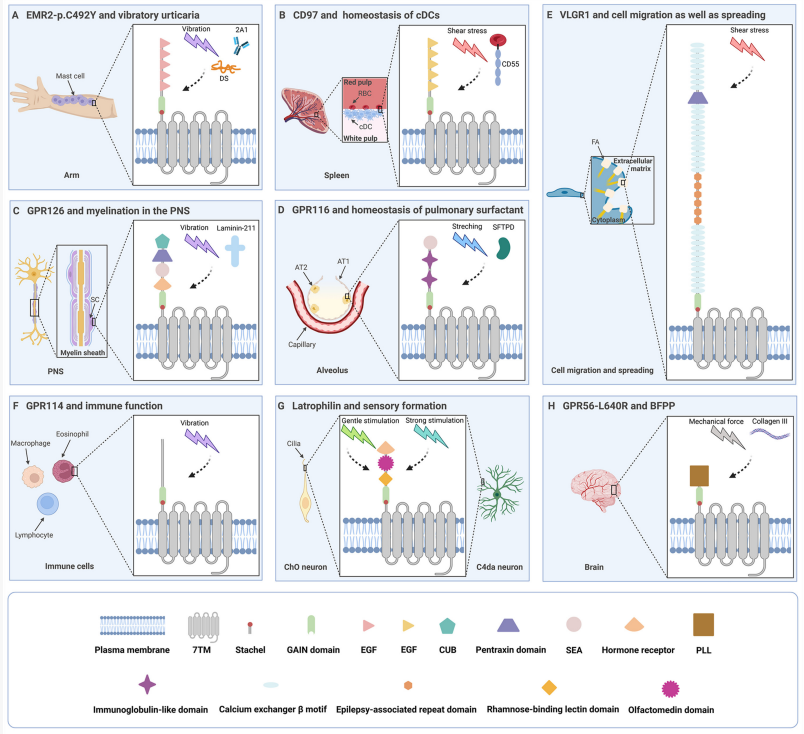
Unlocking the Power of Mechanosensitive Adhesion G Protein-Coupled Receptors in Health and Disease

SHANNON, CLARE, IRELAND, March 4, 2025 /EINPresswire.com/ -- This newly published analysis in Genes & Diseases sheds light on the crucial role of mechanosensitive adhesion G protein-coupled receptors (aGPCRs) in regulating biological processes and their implications in various diseases. These unique receptors translate mechanical stimuli into biochemical signals, influencing cell behavior, development, and disease progression.



Structure and the tethered activation mechanism of aGPCRs. (A) The basic structure of aGPCRs.

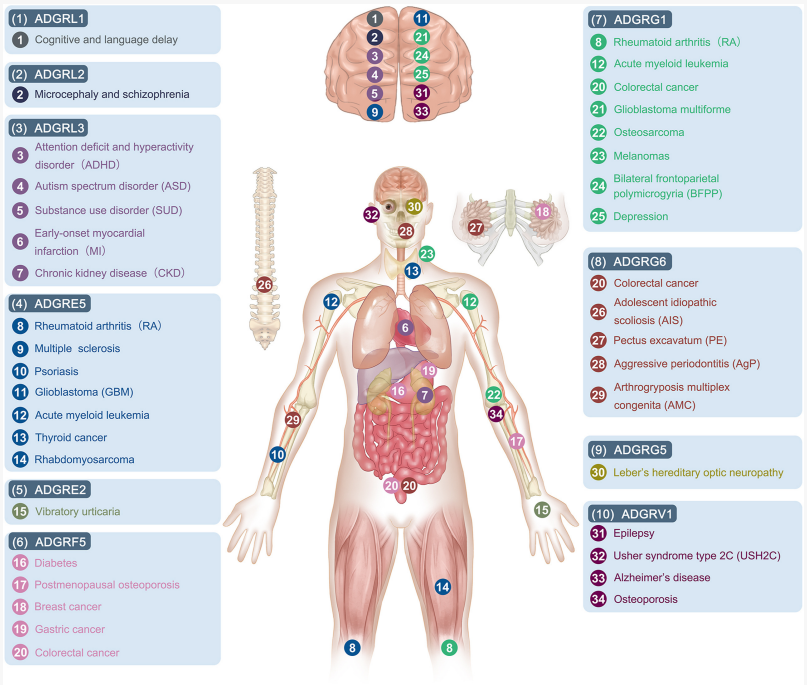


Structures of mechanosensitive aGPCRs and their participation in typical physiological and pathological processes.

As a distinct subgroup of the GPCR superfamily, aGPCRs possess a specialized extracellular domain, enabling them to sense mechanical forces and interact with the extracellular environment. The article highlights how these receptors participate in tissue homeostasis, immune response, neuronal function, and cancer progression. Their ability to respond to shear stress, compression, and cross-linking forces makes them pivotal in both normal physiology and pathological conditions.

Recent insights into their activation mechanisms reveal two primary models: dissociation-dependent activation, where receptor fragments separate to initiate signaling, and non-dissociation

activation, where conformational shifts trigger downstream effects. This distinction underscores the versatility of aGPCRs in adapting to mechanical cues. Their roles extend from modulating platelet aggregation and regulating myelination to controlling surfactant homeostasis in the lungs.



Diseases associated with mechanosensitive adhesion G protein-coupled receptors (aGPCRs). Different colors are used to distinguish diseases related to different receptors.

Beyond their physiological functions, aGPCR dysregulation is increasingly linked to disease. These receptors are implicated in conditions such as cancer metastasis, immune disorders, neurological diseases, and connective tissue abnormalities. For example, mutations in ADGRG1/GPR56 contribute to bilateral frontoparietal polymicrogyria, a severe brain disorder, while ADGRG6/GPR126 mutations are associated with skeletal deformities such as adolescent idiopathic scoliosis. Meanwhile, ADGRE2 dysfunction has been identified as a key factor in vibratory urticaria, a rare hereditary skin disorder triggered by mechanical stimulation.

The therapeutic potential of targeting aGPCRs is vast, given their role in multiple disease pathways. The ability to manipulate these receptors through synthetic ligands or mechanical interventions opens new avenues for precision medicine and drug discovery. With ongoing advancements in structural biology and molecular signaling, a deeper understanding of aGPCR function could lead to innovative treatments for currently untreatable conditions.

This article highlights the critical role of mechanosensitive aGPCRs in human health and disease, setting the stage for future research into mechanotransduction-targeted therapies.

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Genes & Diseases Editorial Office
Genes & Diseases
+ +86 23 6571 4691
editor@genesndiseases.com
