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STUDY OF ALPHA-2A ADRENERGIC RECEPTOR GENE-VARAINTS: FOCUSING ON HUMAN AND RAT ALPHA-2A ADRENERGIC RECEPTOR GENE-VARIANTS.

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A receptor is a protein molecule, embedded in either the plasma membrane or the cytoplasm of a cell, to which one or more specific kinds of signaling molecules may attach. In modern drug development receptors in plasma membrane play an enormous role as targets for a variety of drugs. Contemporary drug testing often involves screening potential drug materials on rat or mice. Final target for these materials is usually human. Previously we have found essential differences in ligand binding properties to human and rat α2A-adrenergic receptor[1]. The reasons for these differences, which where even up to two orders of magnitude, are poorly understood and have to be taken into account in drug development and design.

The aim of current study is to create and implement a stable assay system for studying rat and human variants of α2A-adrenergic receptor in similar environment. For this we would like to use virus-like particles (VLPs) as receptor carrier materials. This method uses VLPs, derived from retroviruses, for purifying and concentrating receptors together with other essential proteins and membrane components from mammalian cells. The obtained material has to be uniform, stable and its production reproducible.

Retrovirus VLPs, being structural part of a virus without genome, are non-infectious and efficacious nanomaterials that take membrane proteins from the cell during budding. The orientation of membrane proteins is the same as in the host cell, in contrast the membrane proteins inserted into artificial vesicles. VLPs produced are quite homogeneous in size and are thus better applicable for different measurement methods.

With changing retrovirus structure we can change the size of the formed particles and thus select proteins that come along with particle (for example effector proteins).

References

1. Oliver Pulges, Ago Rinken. a2A-Adrenoceptor-specific stimulation of [35S]GTPgS binding to membrane preparations of rat frontal cortex. Neurochemical Research, 2008, 33(3) ,477-82.