ARBs bind AGRT1

Jassal, B., Toomey, JR.
Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references


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The vasoconstricting actions of the peptide angiotensin II (AGT(34-41)) are mediated by type 1 angiotensin II receptors (AGTR1), which belongs to class A/1 G protein-coupled receptors (GPCRs). Angiotensin II receptor blockers (ARBs, also known as angiotensin II receptor antagonists, AT1 receptor antagonists or sartans) are a group of pharmaceuticals that modulate the renin–angiotensin system (RAS). ARBs block the activation of AGTR1 receptors, preventing the binding of angiotensin II. Blockage of AGTR1 receptors directly causes vasodilation, reduces secretion of vasopressin, and reduces production and secretion of aldosterone. These combined effects reduce blood pressure by reducing peripheral vascular resistance usually without a rise in heart rate (Israili 2000, Unger 2001). ARBs are primarily used for the treatment of hypertension where the patient is intolerant of ACE inhibitor therapy but also for diabetic nephropathy (kidney damage due to diabetes) and congestive heart failure. ARBs do not inhibit the breakdown of bradykinin or other kinins, and are thus rarely associated with the persistent dry cough or angioedema that limit ACE inhibitor therapy.

Losartan (Cozaar) was the first successful ARB drug, approved in the United States in 1995. It is primarily used to treat hypertension (Goldberg et al. 1995, Mallion & Goldberg 1996) but can also be used to treat diabetic kidney disease (Ruliope & Segura 2003) and congestive heart failure (Konstam et al. 2009). Irbesartan (Avapro) is indicated for the treatment of hypertension, to delay progression of diabetic nephropathy and for the reduction of renal disease progression in patients with type 2 diabetes (Gialama & Maniadakis 2013). Olmesartan medoxomil (Benicar) is an ester prodrug which is completely and rapidly hydrolyzed to the active form, olmesartan (RNH-6270) (Brunner 2002). Olmesartan is indicated for the treatment of hypertension, alone or in combination with other antihypertensive agents. The prodrug candesartan cilexetil is hydrolysed to the active form candesartan (Ishizuka et al. 2013). It is indicated for hypertension and congestive heart failure (Zheng et al. 2011).

Valsartan (Diovan) is mainly used for the treatment of hypertension (Black et al. 1997), congestive heart failure, and to increase survivability after a heart attack (Cohn et al. 2001). Eprosartan (Teveten) is used for the treatment of hypertension (Sega 1999) and is generally better tolerated than enalapril (an ACE inhibitor), especially among the elderly (Ruliope et al. 2001). Telmisartan (Micardis) is indicated in the treatment of essential hypertension and possesses a long duration of action (Littlejohn et al. 2000). Forsartan (compound SC-52458) is sparingly used in the treatment of hypertension because of its short duration of action and being less potent than losartan (Hagmann et al. 1997).
Literature references


Editions

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