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NEW TARGETS OF THE RENIN SYSTEM FOR FUTURE DRUGS

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The Renin-angiotensin system (RAS) system plays a central role in the control of blood pressure in the body. This report focuses on new drugs that has the possibility to replace the roles of the present drugs that treat hypertension.

Blockers of RAS, particularly ACE inhibitors, have greatly impacted clinical medicine, especially in cardiovascular health. They are recommended as first-line treatment for heart failure and hypertension. RAS inhibitors have common side effects such as functional renal insufficiency, development of hyperkalemia, and onset of anemia. Patients taking ACE inhibitors still face higher risks of cardiovascular issues and early death.

Arora et at. studied 678 patients with an eGFR below 30mL/min/1.73m^2 categorizing RAS blockers use into four groups: always users, never users, dynamic users. They found no significant differences in kidney failure or mortality risk among these groups.

Research on new parts of the renin- angiotensin system and its function has led to potential new treatments that may improve blood pressure control and reduce side effects

Combining therapies or using dual-acting agents can enhance effectiveness. Focus is now on novel therapies in early development stages, including small molecule inhibitors, receptor agents, gene therapy, recombinant ACE2 and designer peptides targeting RAS for better management of hypertension and heart failure.

Angiotensin II receptor subtypes: Another enzyme that contributes to the conversion of angiotensin I to Ang 1-9, which helps mitigate cardiovascular damage. Research shows Ang 1-9 offers protective effects in heart conditions by counteracting detrimental modelling and hypertrophy.

Angiotensin Peptides: Like Ang 1-7 have unique beneficial effects, including vasodilation and anti-inflammatory actions. Ang 1-7 is generated through cleavage of angiotensin peptides and has been linked to improved cardiovascular health.

Kinin system: An important hormonal pathway that helps to balance overactive Renin-Angiotensin system. Bradykinin is a key vasodilator produced by Kallikrein, promoting vasodilation and inflammation. Two receptors, B1R and B2R, respond to injury and vasodilation, respectively. ACE inhibitors increase bradykinin levels, lowering blood pressure but may cause side effects like cough and angioedema.

Endothelin Receptor Antagonists: Although not directly part of RAAS, endothelin interacts with the system and contributes to vascular tone and remodeling. The endothelin system regulates blood pressure and blood vessels by producing endothelin-1 (ET-1) which constricts blood vessels. It interacts with RAS system and is targeted for hypertension and heart failure treatment, but medications may cause side effect. The regulation of these hormones involves enzymes and receptors affecting their production and breakdown.

Neprilysin inhibitors: Neprilysin is an enzyme that breaks down Natriuretic peptides, Bradykinin and Angiotensin II. Inhibiting Neprilysin can enhance the levels of these beneficial peptides, leading to vasodilation and natriuresis.

Overall Angiotensin peptides and Neprilysin inhibitor may offer the most innovative and beneficial approaches due to their ability to enhance protective.