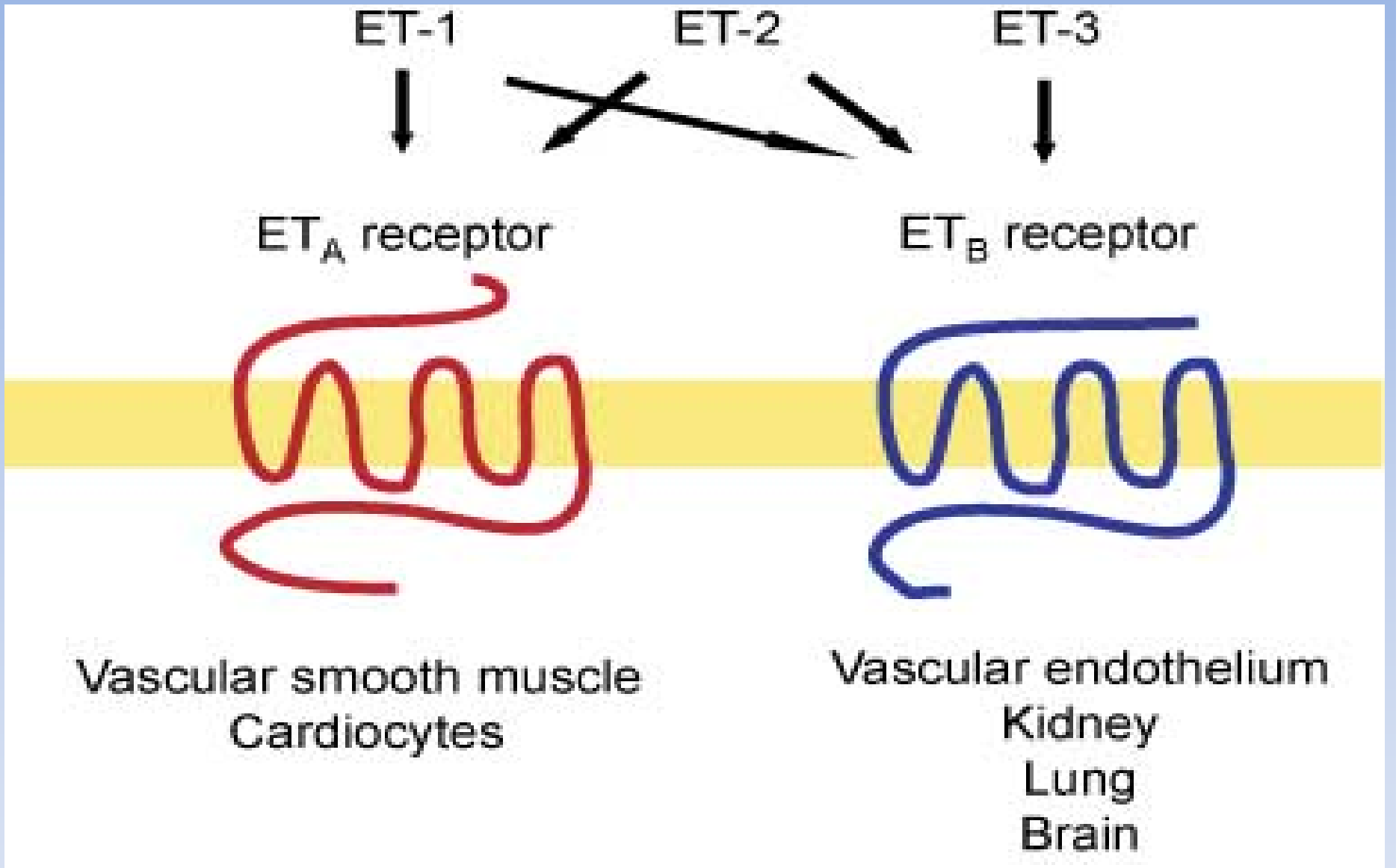
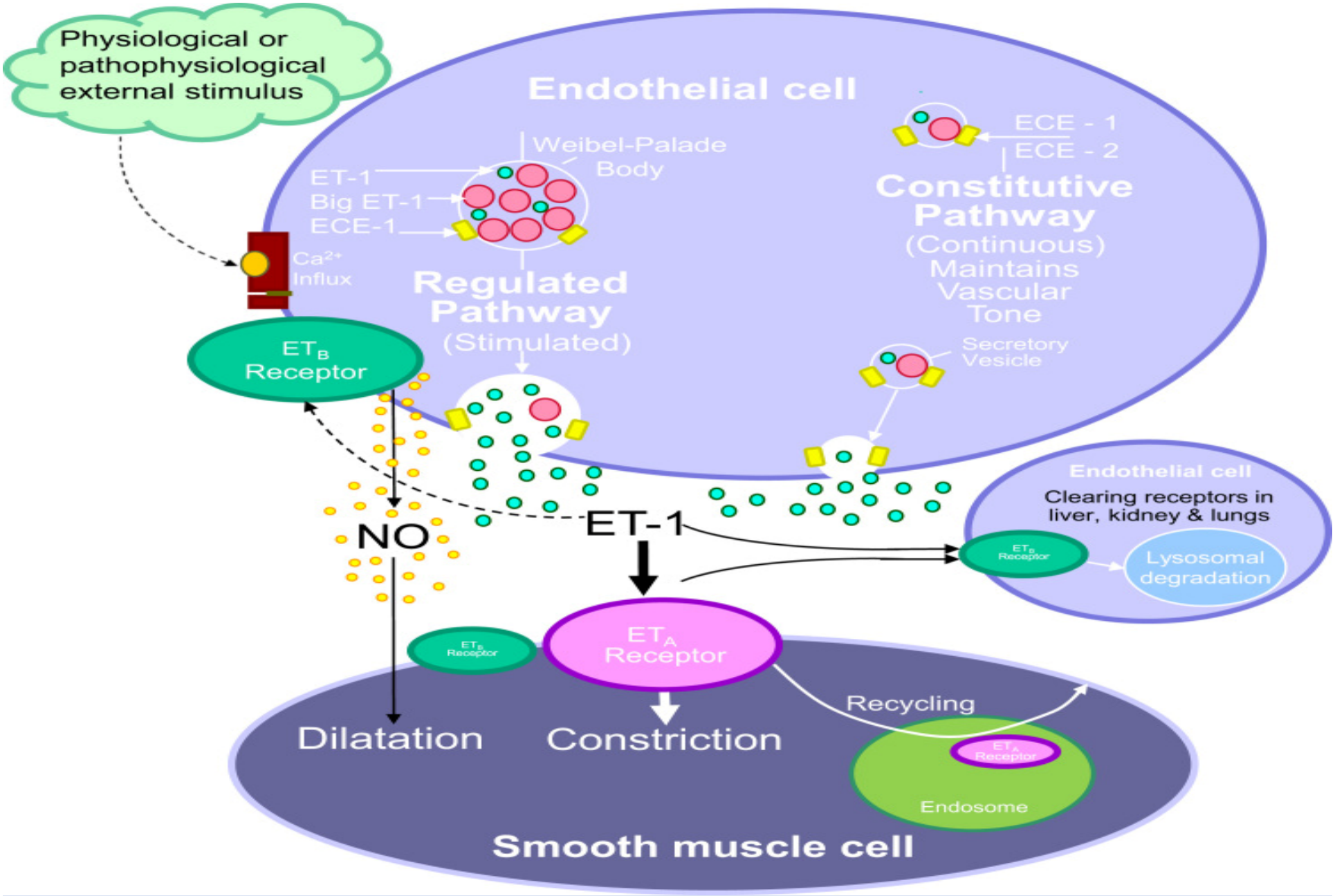
ENDOTHELİN RECEPTORS

Prof.Nuray ARI, 2018



Koyama Y. BioMolecular Concepts, 4 (4):335–347, 2013



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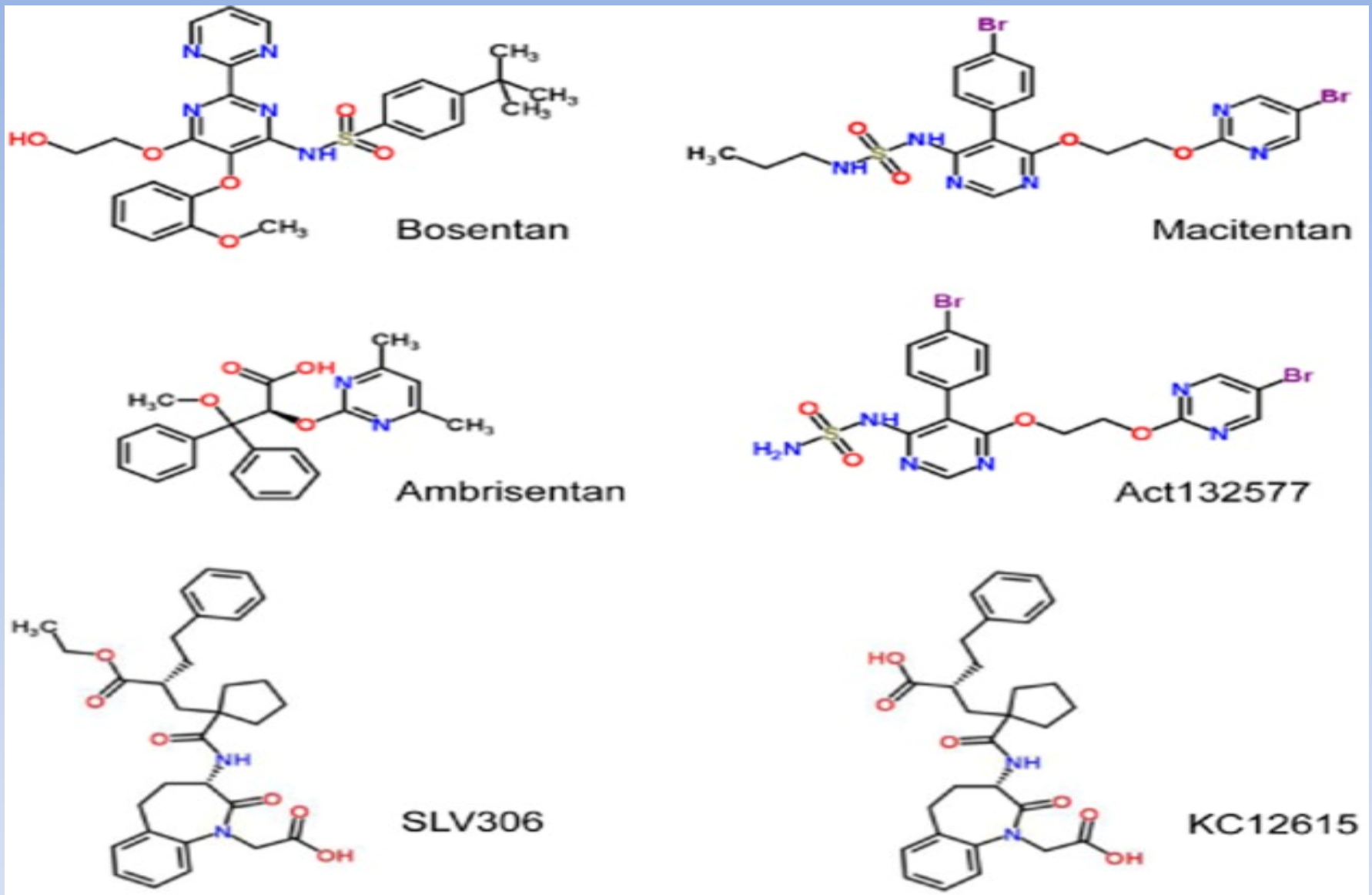
Maguire JJ, and Anthony P. Davenport AP. Semin Nephrol. 2015, 35(2): 125–136

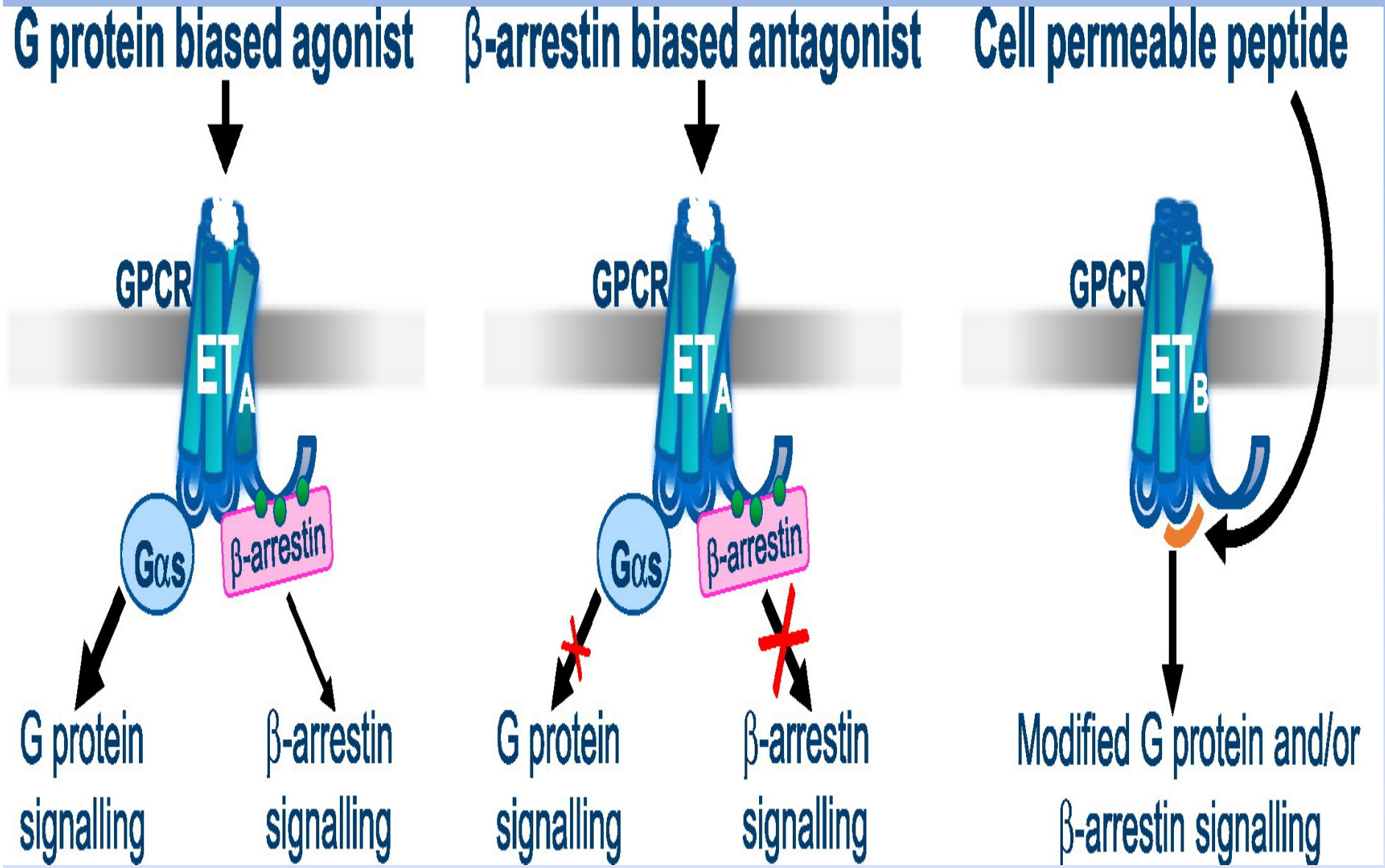


Structures of ET receptor antagonists in clinical use bosentan, ambrisentan and macitentan. The structures of the NEP/ECE inhibitor pro-drug SLV306 and its active metabolite are also shown.

J J Maguire, A P Davenport. Br J Pharmacol. 2014, 171(24): 5555–5572.

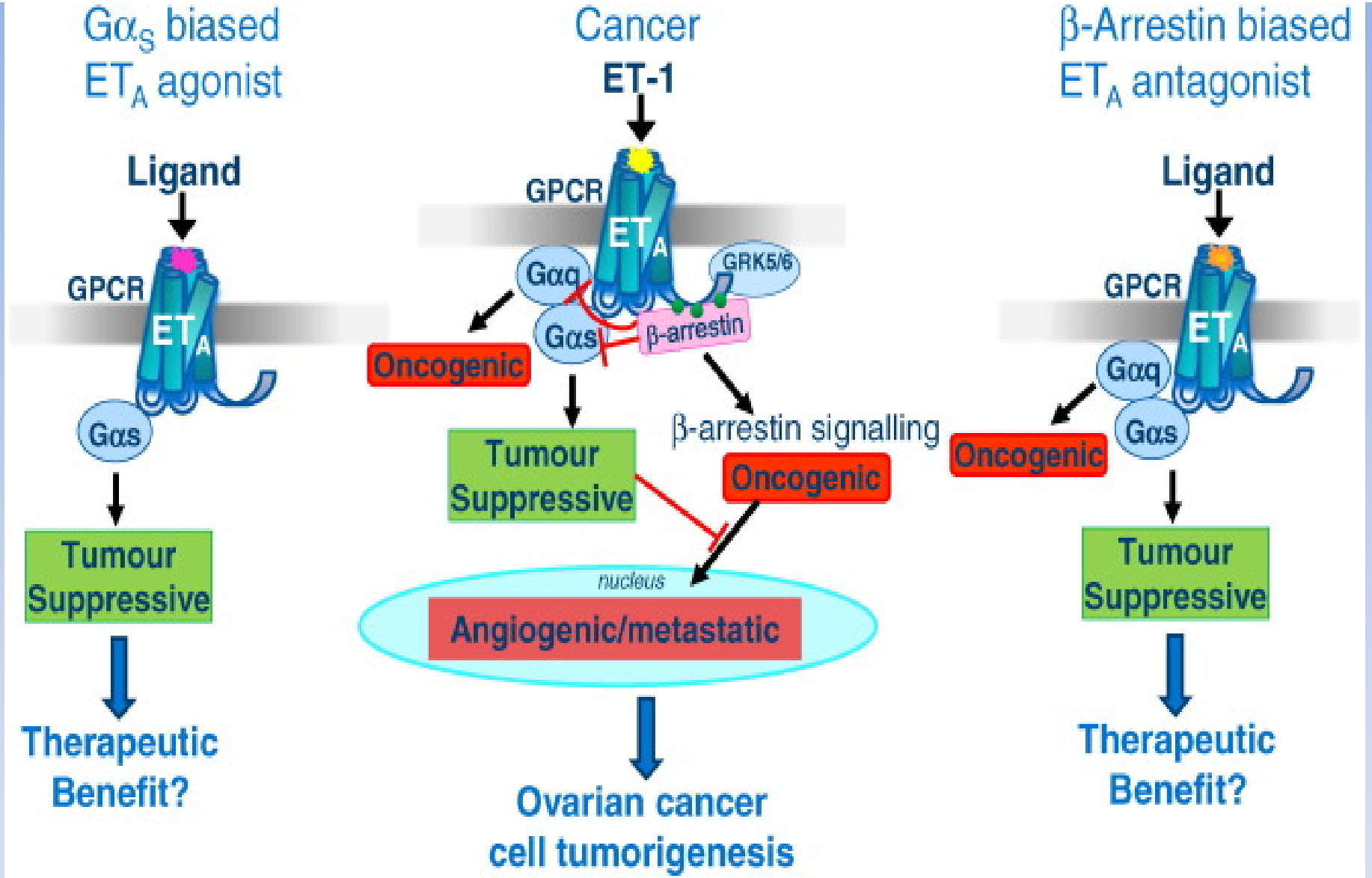
- Life Sci. 2016 Aug 15;159:30-33. doi: 10.1016/j.lfs.2016.02.069. Epub 2016 Feb 17.
- **Evidence for biased agonists and antagonists at the endothelin receptors.**
- Maguire JJ.

- Abstract
- Biased ligands represent a new strategy for the development of more effective and better tolerated drugs. To date there has been a paucity of research exploring the potential of ligands that exhibit either G protein or β-arrestin pathway selectivity at the endothelin receptors. Re-analysis of data may allow researchers to determine whether there is existing evidence that the endogenous ET peptides or currently available agonists and antagonists exhibit pathway bias in a particular physiological or disease setting and this is explored in the review. An alternative to molecules that bind at the orthosteric site of the ET receptors are cell penetrating peptides that interact with a segment of an intracellular loop of the receptor to modify signalling behaviour. One such peptide IC2B has been shown to have efficacy in a model of pulmonary arterial hypertension. Finally, understanding the molecular pathways that contribute to disease is critical to determining whether biased ligands will provide clinical benefit. The role of ETA signalling in ovarian cancer has been delineated in some detail and this has led to the suggestion that the development of ETA G protein biased agonists or β-arrestin biased antagonists should be explored.



Pathway bias at the ET receptors.

Life Sciences, 159:30-33,2016. Maguire JJ



Proposed role for ET-1 activation of ET_A receptors in ovarian cancer and potential beneficial effects of either a $G_\alpha s$ biased agonist or β-arrestin biased antagonist.

Life Sciences, 159:30-33,2016. Maguire JJ