

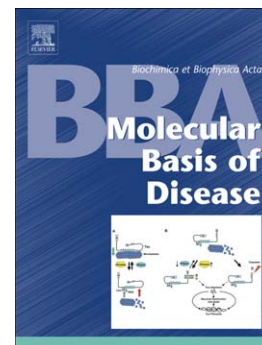
Accepted Manuscript

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PII: S0925-4439(17)30274-0  
DOI: doi:[10.1016/j.bbadis.2017.08.001](https://doi.org/10.1016/j.bbadis.2017.08.001)  
Reference: BBADIS 64851

To appear in: *BBA - Molecular Basis of Disease*



Please cite this article as: Ya-Xiong Tao, Melanocortin Receptors, *BBA - Molecular Basis of Disease* (2017), doi:[10.1016/j.bbadis.2017.08.001](https://doi.org/10.1016/j.bbadis.2017.08.001)

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## Melanocortin Receptors

Melanocortins, primarily consisting of  $\alpha$ -melanocyte stimulating hormone (MSH),  $\beta$ -MSH,  $\gamma$ -MSH, and adrenocorticotropin (ACTH), are small peptide hormones derived from tissue-specific post-translational processing of a pre-prohormone, proopiomelanocortin (POMC). In the skin and brain (including the hypothalamus and hindbrain), POMC is processed to the MSHs by the combined action of prohormone convertase 1 and 2 whereas it is processed to ACTH by prohormone convertase 1 in the anterior pituitary gland.

Extensive studies spanning several decades have elucidated well-established functions of melanocortins on pigmentation and adrenal steroidogenesis. These functions are mediated by cell surface receptors that are coupled to the stimulatory heterotrimeric G protein, G<sub>s</sub>. With the cloning of the classical MSH receptor and ACTH receptor, it was soon realized that three additional G protein-coupled receptors (GPCRs) with significant homology to the MSH receptor and ACTH receptor exist in mammalian genomes. The five cell-surface GPCRs that mediate melanocortin action are named MC1R (MSH receptor), MC2R (ACTH receptor), MC3R to MC5R, based on the sequence of their cloning.

The cloning of the five MCRs ushered in a new exciting era of research in the physiology, pharmacology and pathophysiology of the MCRs. New physiological functions were identified. For example, in addition to its well-known function in regulating pigmentation, the MC1R is also an important regulator of inflammation with significant therapeutic implication for diverse inflammatory diseases. The studies on the gene expression of the then-newly

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