



Genetic Steroid Disorders: Chapter 11. Nuclear Receptor Co-regulators

David M. Lonard, Bert W. O'Malley

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Nuclear receptors are transcription factors that bind steroid, retinoid and thyroid hormones, and other ligands to drive hormone-dependent gene expression in conjunction with co-activators and co-repressors, collectively referred to as co-regulators. So far, more than 400 co-regulators have been reported in the literature and they have been implicated in a wide variety of pathological conditions, genetic syndromes, and in cancer. A key feature of co-regulator-based disease is the pleiotropic effects that disruption of normal co-regulator function has on energy metabolism, neurological function, and susceptibility to cancer. Technological advances in proteomics, genomics, and transcriptomics are leading to new ways to understand the pleiotropic actions of co-regulators. We expect that co-regulator 'omics' will lead to ways of understanding how co-regulators can be evaluated in the context of other complex genetic factors, hormones, diet, the environment, and stress. The broad role that co-regulators have in human pathological conditions makes it important to consider them as important new drug targets, such as for the treatment of hormone-dependent cancers or for indications related to energy metabolism. Better system-wide knowledge of co-regulator control of transcription and physiology is expected to lead to the best placement for future co-regulator-based therapies.

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