Sex Hormones and Gender-Specific Signal Transduction: Research Perspectives and Implications for Therapeutic Strategies

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Numerous clinical observations and epidemiological studies clearly indicate gender-specific variations in occurrence and severity of major common gender-neutral diseases with prominent socio-economical impact, such as colon cancer [1-3], obesity [3,4], multiple sclerosis [5,6], kidney [7], bone [8], degenerative [9] and cardiovascular [3,10,11] disorders. Such gender-specific dimorphism observed in humans has been confirmed in experimental studies on animal models of some common human diseases. These clearly indicate that sex hormones may influence predisposition to and development of a wide range of common pathological conditions. Therefore, it is conceivable that sex hormones may also differentially affect the action of drugs and efficacy of therapeutic strategies in treatment of those conditions.

Sex steroid hormones influence crucial physiological processes through the genomic actions of their cognate nuclear receptors. Recent studies suggest that sex steroids may also exert their effect through rapid-response mechanisms resembling known membrane receptor-mediated signaling and activation of various kinases [12,13]. Complexity of the sex hormone physiological effects further increases owing to the convergence of the sex steroid signaling with many other important signaling pathways (as different as arylhydrocarbon [14], wnt [15], leptin [16] signal transduction, just to name a few) through molecular interaction between the downstream mediators.

Progress in molecular biological and genetic studies on mechanisms of signal transduction led to identification of key mediators of major signaling pathways relevant to etiology of most prevalent human diseases. At the same time, activities of disorder-relevant pathway mediators are often therapeutically targeted in treatment of various common metabolic disorders. Taken together, these open possibilities of determination of gender-specific effects of already approved or novel up-coming pharmaceutical compounds and optimization of their use to develop gender-specific therapeutic strategies in treatment of common human diseases.

References


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