Signal Transduction pathways steroidal

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Steroid hormones, i.e., androgens, estrogens, glucocorticoids, mineralocorticoids, and progestins, bind with high affinity to their respective steroid hormone receptors (SR). SRs are members of a family of nuclear receptors (NR). Ligand-activated SRs dissociate from hsp90 chaperone complexes in the cytoplasm and enter the nucleus where they bind to specific DNA sequences: hormone response elements (HREs). SRs interact with coregulator proteins (coactivators and corepressors) as well as chromatin remodeling complexes to regulate target gene expression. In addition, some SRs are also associated with the plasma membrane (PM) and PM proteins. Hormone binding to PM-associated SRs activates G-protein coupled receptors (GPCR) and intracellular signaling pathways ultimately regulating gene transcription and other downstream sequelae. This chapter will review of SR/NR including protein structure, ligand activation, gene regulation, examples of rapid “non-genomic” signaling, and the roles of these receptors in human health and disease.

Classical steroid hormones (SHs) - estrogens, androgens, progestins, glucocorticoids and mineralocorticoids - play critical roles in the regulation of reproduction, metabolism and cancer. SHs act via their cognate steroid hormone receptors (SHRs) in multiple target tissues throughout the body, exerting their physiological effects through nuclear receptor (NR)-mediated gene transcription. Since SHRs are the mediators of steroid hormone signalling in cells, regulation of their expression and function is critical for appropriate physiological responses to SHs. Cells regulate SHRs by determining the cellular concentration of SHR proteins in the cell and by tightly regulating their activity through post-translational modifications and interactions with coactivator protein complexes. In this chapter we will examine each of these regulatory mechanisms and assess their functional impact on the activity of SHRs.

Hormones exert powerful effects on reproductive physiology by regulating gene expression. Recent discoveries in hormone action emphasize that regulation of gene expression is not restricted to their alterations of the rate of gene transcription. On the contrary, hormonal effects on the stability of a specific mRNA can profoundly alter its steady-state concentration. The mRNAs encoding hormone receptors are commonly regulated by their own hormones to create autoregulatory feedback loops. Negative and positive autoregulatory feedback loops serve to limit or augment hormonal responses, respectively. After introducing the topics of mRNA degradation and regulated stability, this review focuses on steroid hormone effects on mRNA stabilities. Autoregulation of the mRNAs encoding estrogen, progesterone, androgen, and glucocorticoid receptors by the steroid hormones in reproductive tissues is discussed. In addition, steroid hormone effects on the stabilities of many other mRNAs that are important to reproductive biology are reviewed. These include mRNAs that encode gonadotropin hormones,

integrins, growth factors, and inflammatory response proteins. Through these posttranscriptional effects, steroid hormones impact the expression of a large population of genes. Studies of the molecular mechanisms of hormonally regulated mRNA stabilities continue to identify critical mRNA sequence elements and their interactions with proteins. Increased understanding of how hormones affect mRNA stability may yield novel approaches to the therapeutic control of hormone effects, including those essential to reproductive physiology in animals.

Leucine-rich repeat receptor kinases in plants: structure, function, and signal transduction pathways

Transmembrane receptor kinases (RKs) mediate signal transduction pathways leading to cell proliferation, growth, and diVerentiation in animals. The crucial function of RKs is recognition of an extracellular ligand, which leads to activation of the intracellular kinase domain and subsequent transduction of downstream signaling pathways. The completion of Arabidopsis genome sequencing revealed a surprisingly high number of genes (at least 610 members) encoding putative receptor kinases, which strongly suggests that the plant cells predominantly use RKs for sensing external signals and regulating gene expression. Plant RKs comprise a monophyletic group related to animal RKs. Almost all plant RKs phosphorylate serine/threonine residues, unlike animal RKs, are predominantly ligand-activated tyrosine kinases (Shiu and Bleecker, 2001a, b). The plant RKs are often referred to as ''receptor-like kinases (RLKs),''because their corresponding ligands have yet to be identified with the exception of a few.

Plant RKs are classified into several groups based on the structure of the extracellular domains. RKs containing an extracellular leucine-rich repeat (LRR) motif comprise by far the largest subfamily of plant RKs, with $222 members in the Arabidopsis genome (Fig. 1)(Shiu and Bleecker, 2001b; Yin et al., 2002b). Consistently, LRR-RKs are some of the most extensively studied and well-understood signaling molecules in plants. For instance, growing numbers of LRR-RKs whose loss-of-function mutations confer phenotypes convincingly show that they play fundamental roles in development, steroidhormone response, stress response, disease resistance, and symbiosis (Bishop and Koncz, 2002; Gomez-Gomez and Boller, 2002; Jones and Jones, 1997; Kistner and Parniske, 2002; Torii, 2000; Torii and Clark, 2000). Furthermore, identification of ligand molecules for several LRR-RKs led to breakthroughs in our understanding of peptide and steroid hormone signal transduction in plants. This review provides an updated, comprehensive view of structure, function, modes of action, and signal transduction pathways mediated by plant LRR-RKs, including the nature of ligand molecules, factors that modify ligands, and downstream components, for the aim of deciphering their conserved and specific roles in development and environmental response.

Peptide hormones released from the anterior pituitary bind to specific receptors on a limited number of cell types (steroidogenic cells). Signals resulting from this binding are amplified through the produc-tion of steroid hormones, leading to the regulation of transcription of genes in all cells. A major advancement in biology has been the identification and characterization of nuclear receptors that bind specific ligands, forming complexes that bind to specific DNA sequences through their zinc finger motifs and thereby regulating transcription of the associated genes. Levels of one class of ligands, the steroid hormones, are controlled by the action of peptide hormones from the anterior pituitary. Over the same period of time that the nuclear steroid hormone receptors have been characterized, an understanding of the regulatory processes leading to production of these steroidal ligands has emerged. Consequently, we now have a good view of how these peptide hormones exert their actions. Adrenocorticotropin (ACTH) receptors are found in the adrenal cortex, luteinizing hormone (LH) receptors in the testis and ovary, and follicle-stimulating hormone (FSH) receptors in the ovary. Each of these endocrine tissues is a factory for production of a specific subset of steroid hormones. In this way the endocrine roles of the adrenals and gonads serve to amplify

The substrate-specific protein chaperone Hsp90 (heat shock protein 90) from Saccharomyces cerevisiae functions in diverse signal transduction pathways. A mutation in YDJ1, a member of the DnaJ chaperone family, was recovered in a synthetic-lethal screen with Hsp90 mutants. In an otherwise wild-type background, the ydj1 mutation exerted strong and specific effects on three Hsp90 substrates, derepressing two (the estrogen and glucocorticoid receptors) and reducing the function of the third (the tyrosine kinase p60v-src). Analysis of one of these substrates, the glucocorticoid receptor, indicated that Ydj1 exerts its effects through physical interaction with Hsp90 substrates.

Small signaling molecules that mediate cell–cell communication are essential for developmental regulation in multicellular organisms. Among them are the steroids and peptide hormones that regulate growth in both plants and animals. In plants, brassinosteroids (BRs) are perceived by the cell surface receptor kinase BRI1, which is distinct from the animal steroid receptors. Identification of components of the BR signaling pathway has revealed similarities to other animal and plant signal transduction pathways. Recent studies demonstrated that tomato BRI1 (tBRI1) perceives both BR and the peptide hormone systemin, raising new questions about the molecular mechanism and evolution of receptor–ligand specificity.

Mechanisms of ovarian steroid regulation of norepinephrine receptor-mediated signal transduction in the hypothalamus: implications for female reproductive physiology

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In many mammalian species, the ovarian steroid hormones estradiol (E2) and progesterone (P)

act in the hypothalamus and preoptic area to coordinate the timing of female sexual receptivity with ovulation. We study lordosis behavior, an important component of sexual receptivity in rats, and its regulation by E2 and P as a model system for understanding how hormonal modulation of synaptic neurotransmission influences reproductive physiology and behavior. Our findings suggest that E2 and P extensively regulate synaptic communication involving..

Membrane receptors for steroid hormones affect signaling pathways that modulate nuclear function, influence neuronal activity, ion flow, and the circulatory system. Indeed, 'new' steroid hormones have been identified by their interaction with membrane-initiated signaling systems. A brief summary of the FASEB Summer Research Conference devoted to these topics is presented in this mini-review. In addition, attendees of the meeting propose introduction of the following terminology: membrane-initiated steroid signaling (MISS) and nuclear-initiated steroid signaling (NISS) to replace more inaccurate terms in current use.

For a disease such as cancer, where a number of alterations to normal cell function accumulate over time, there are several opportunities to inhibit, slow down or even reverse the process. Many of the changes which drive the disease process occur in cell-signalling pathways that regulate proliferation and apoptosis. As our knowledge of these complicated signalling networks improves, it is becoming clear that many molecules, both drugs and naturally occurring dietary constituents, can interact beneficially with deregulated pathways. Aspirin and other non-steroidal anti-inflammatory drugs, as well as natural compounds present in plants such as green vegetables and tea, can modulate signalling by affecting kinase activity and therefore phosphorylation of key molecules. Examples of pathways which can be modulated by these agents include activation of the transcription factor nuclear factor κB by tumour promoters or cytokines, signalling by growth factors through the growth-factor receptor/extracellular-regulated protein kinase pathways and by a number of other molecules through the stress-activated c-Jun N-terminal kinase and p38 pathways. These mitogen-activated protein kinase pathways regulate a number of transcription factors including c-Fos and c-Jun. Evidence exists, at least from in vitro experiments, that by targeting such pathways, certain dietary compounds may be able to restore abnormal rates of apoptosis and proliferation to more normal levels.