

# STEROID-INDEPENDENT ACTIVATION OF STEROID RECEPTORS

Factor <sup>a</sup>	ER <sup>b</sup>	PR <sup>c</sup>	AR
ATP	1		
Dopamine	2	2	
Epidermal growth factor (EGF)	3,4	5	6
erbB2 = HER-2	7		8
Fibroblast growth factor 2 (FGF-2 = bFGF)	9		
Gas-6			10
Gonadotropin release hormone (GnRH)	11	12	
GRP			10
Heregulin	7	13	10
Insulin and insulin-like growth factors (IGF)	14-16		6
Interleukin-6	17		18,19
Interleukin-8			20
Keratinocyte growth factor			6
Leptin	21		
Prolactin	22		
Sex hormone binding globulin			23
TGF $\alpha$	4		
TNF $\alpha$	24		
Amino acids (through mTOR and S6K)	25		
Cdk2		26	
Cyclin A-Cdk2	27		
Cyclin D1	28,29		
Ets-1	30		
Hif-1 $\alpha$ (hypoxia)	31		
IKK $\epsilon$	32		
MAPKK (constitutive mutant)	33		
MEKK1 (constitutive mutant)			34
Pak1	35		
PI3K	36		
PKC $\delta$	37		

Protein kinase B (= Akt)	36,38-40		
Ras (constitutive mutant)	41		
v-Src	42		
Vav3 (a Rho GEF)	43		44
Activators of protein kinase A	14,45	46	47
Activator of protein kinase C	37,41,48		49
Caffeine	1		
Calcium	1		
Inhibitors of protein phosphatases 1 and 2A	2	2,46	
Inhibitor of phosphotyrosine phosphatases		5	
Metals, arsenite, selenite	50-53		

- <sup>a</sup> This list may be incomplete as the extent of steroid-independent activation varies widely; moreover, several reports have indicated that some of the effects may be cell- and/or promoter-specific (see for example ref. 8,54).
- <sup>b</sup> Almost all publications have examined ER $\alpha$ . ER $\beta$  has only been shown to be activated by EGF (55,56) and indirectly by 3,3'-diindolylmethane (57).
- <sup>c</sup> The response of PR displays marked species differences: chicken and rodent PRs can be activated in the absence of cognate hormone by a whole series of activators that will only affect human PR in the presence of a ligand, for example the partial antagonist RU486 (refs. 58-60; exceptions to the rule are the activation of human PR by heregulin [13] and Cdk2 [26]).

Note:

- other steroid receptors, notably GR and MR, are more restricted in their ability to be activated in the absence of ligands. A noteworthy "exception" is the activation of GR by GnRH and TNF $\alpha$  signaling (61,62).
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