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Other miscellaneous hormone binding proteins: Attempt at an epilogue

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ABSTRACT

An overview of the detection, mechanism of formation and clinical function of hormone binding proteins shedded from the membrane receptor and detected in the last twenty years is presented. The representatives of such binding proteins are restricted only to human soluble receptors that have been already detected in blood or other intravasal fluids such as soluble receptors for LH/hCG, prolactin, TSH, erythropoietin, insulin and IGF-I. The clinical or diagnostic significance of these putative-detectable or indeed circulating proteins often remains largely unclear.

The aim of this issue of *Best Practice and Research Clinical Endocrinology and Metabolism* was to summarize recent investigations into the different faces of hormone-binding proteins. The focus is not only on classical binding proteins that are encoded by a specific gene, but also on binding proteins that have their origin in hormone membrane receptors. These receptors are either shed from the extracellular membrane to generate soluble isoforms or they are derived by translation from a differently spliced mRNA. In some rare cases, both routes have been described for the formation of binding proteins.

As mentioned in the individual chapters, most representatives of classical hormone binding proteins, such as carriers for thyroid hormones, glucocorticoids, sexual hormones and vitamin D, were firstly detected about 50 years ago. Interestingly, almost no clinically relevant additional binding

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Table 1
Human hormone-binding proteins not described in the previous chapters.

References	Medium, method of detection	Biochemical characteristics/ formation	Clinical relevance
Soluble receptor for luteinizing and chorion gonadotropic hormone (sLHCG-R)			
Chamber AE et al., 2011a [1]	Supernatant of transfected cells and human placental explants; Western blot	Constitutive secretion via microvesicles	Only speculations about its function as modulator of LH or hCG action
Chamber AE et al., 2011b [2]	Serum, ELISA	Not investigated	Low levels are associated with high and low responders in ovarian stimulation before IVF treatment
Chamber AE et al., 2012 [3]	ELISA, Western blot	Molecular weight: 50, 62 and 75 kD	Together with PAPP-A recognition of patients with Down Syndrome that were negative for PAPP-A plus fbetahCG
Chamber AE et al., 2014 [4]	Serum, ELISA	Not investigated	Increased the detection rate of Down Syndrome together with PAPP-A and fbhCG measurement in first trimester screening by 35%
Soluble prolactin receptor (sProl-R)			
Amit T et al., 1997 [5]	Milk, 125-Iodine specific binding, Cross-linking/SDS-PAGE	Molecular weight: 35 kD in milk	Inhibitor or potentiator, buffer or reservoir of hormone (action), binds also hGH
Bradford Kline J and Clevenger CV, 2011 [6]	Serum, milk; immunoprecipitation, immunoblot, MALDI-mass spectrometry	Molecular weight: 32 kDa, no glycosylation; deglycosylation and proteolysis of the full-length Prol-R	Antagonizes Prol action and Prol-driven growth *in vitro*, binds GH in blood
Soluble thyrotropin receptor (sTSH-R)			
Murakami M et al., 1992 [7]	Plasma; RIA, gel filtration, SDS-PAGE, Western blot	Molecular weight: 60 kDa in human plasma	Significantly higher in Graves diseases than in normal or hypothyroid patients with Hashimoto thyroiditis.
Hunt N et al., 1993 [8]	Radioprecipitation with 125I-TSH and polyetylenglycol	3000 g supernatant of human thyroid homogenate, no sedimentation with membranes	Present in Grave's disease?
Couet J et al., 1996 [9]	Sandwich immunoassay, Western Blot	Molecular weight: 53 kDa, 35 kDa after deglycosylation; reflects the alpha-subunit of TSH-R; shedding of TSH-R from human thyrocytes or transfected CHO and L cells, serum	Stimulation of TSH-R cleavage by TSH in the cell model but no data for clinical relevance
Chazenbalk GD et al., 2004 [10]	Flow cytometry, radiolabeled TSH binding, crosslinking	Transfected CHO cells	No effect of TSH on TSH-R cleavage in the cell model
Soluble erythropoietin receptor (sEpo-R)			
Baynes RD et al., 1993 [11]	Serum; SDS-PAGE, Western blot	Molecular weight: 34 kDa; in human serum and bone marrow cells	Highly correlated with enhanced erythropoiesis, reflects early or total progenitor cell activity.
Soluble insulin receptor (sI-R)			
Pezzino V et al., 1992 [12]	Plasma, RIA, SDS-PAGE, autoradiography	Molecular weight: 135 kDa corresponding to the α subunit of the I-R; 82 kDa with autophosphorylation activity	Plasma high affinity binding activity