Pituitary corticotroph adenoma pathogenesis

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Transcriptome expression

The aim of a study was to evaluate transcriptome expression pattern in a large series of ACTH-secreting pituitary neuroendocrine tumor specimens, in order to identify molecular signatures of these tumors. Gene expression profiling of formalin-fixed paraffin-embedded specimens from 40 human ACTH-secreting pituitary neuroendocrine tumors revealed significant expression of genes involved in protein biosynthesis and ribosome function, in keeping with neuroendocrine cell profile. Unsupervised cluster analysis identified three distinct gene profile clusters and several genes were uniquely overexpressed in a given cluster, accounting for different molecular signatures. Of note, gene expression profiles were associated with clinical features such as age and size of the tumor. Altogether, the study shows that corticotrope tumors are characterized by neuroendocrine gene expression profile and present subgroup-specific molecular features [1)].

History

In 2002 Trouillas published that the specific factors involved and markers of aggressiveness remain to be discovered [2)].

In 2012 Dworakowska et al., searched PubMed on any paper related with molecular pathology of pituitary corticotroph adenomas and included to a review all relevant references published up to June 2011.

Current studies increased our knowledge on the genetic basis of McCune-Albright syndrome (MAS), multiple endocrine neoplasia type 1 (MEN1), Carney complex (CNC), pituitary neuroendocrine tumor predisposition syndromes and tuberous sclerosis, but they have performed little to elucidate the causes of sporadic pituitary tumours including Cushing disease.

The aim of this review was to focus on the most recently published advances in the molecular pathology of corticotroph adenomas, which are presented in the context of changes seen in all types of pituitary neuroendocrine tumors, as well as in terms of corticotrophin-releasing hormone/ACTH/cortisol-specific pathways.

They expected that over the next 5 years, more detailed analysis of inter-cellular communication pathways between pituitary cells, including the cadherins and integrins, and their interactions with other signalling pathways such as the β-catenin cascade will help elucidate what exactly goes awry in the formation of a benign corticotroph adenoma. This should in turn predict novel forms of pharmacological tumour control [3)].

References

1)

Cassarino MF, Ambrogio AG, Cassarino A, Terreni MR, Gentilini D, Sesta A, Cavagnini F, Losa M, Pecori Giraldi F. Gene expression profiling in human corticotrope tumors reveals distinct, neuroendocrine profiles. J Neuroendocrinol. 2018 Jun 19:e12628. doi: 10.1111/jne.12628. [Epub ahead of print] PubMed PMID: 29920815.

2)

Trouillas J. [Pathology and pathogenesis of pituitary corticotroph adenoma]. Neurochirurgie. 2002 May;48(2-3 Pt 2):149-62. Review. French. PubMed PMID: 12058122.

3)

Dworakowska D, Grossman AB. The molecular pathogenesis of corticotroph tumours. Eur J Clin Invest. 2012 Jun;42(6):665-76. doi: 10.1111/j.1365-2362.2011.02621.x. Epub 2011 Nov 19. Review. PubMed PMID: 22098190.