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Tintin's blight

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Tintin never grew up. Readers followed his travels around the world for almost fifty years and yet the Belgian journalist showed no signs of ageing whatsoever. No grey hair, no wrinkles, no loss of stamina. He never changed style either; he never tired of his plus fours or of his cranial crest. How can a human span a lifetime looking as though he never grew older than the age of fifteen? Hypogonadotropic hypogonadism – or HH – say some. HH is a condition in which the afflicted subject never reaches puberty. For a man, this would mean that he shows no signs of becoming one, i.e. he has no facial hair for example nor is he the proud owner of a mature reproductive system. Tintin never took his trousers down, but his readers know that he never showed signs of growing a beard. HH in a man is caused when the regulation of the male hormone, testosterone, is deficient. And we now know of one protein which seems to have a key role in this regulation: the KiSS-1 receptor.

How does a condition like HH occur? It all has to do with hormones. Puberty is triggered off by a flush of hormones, amongst which are those that cause a young boy to grow hair on his chin or a girl to menstruate. If such hormones are hindered in any way, an adolescent will never know the joys of a beard, or a razor. At puberty, a region of our central nervous system, the hypothalamus, releases a hormone known as 'gonadotropin-releasing hormone' which itself causes the release of two other hormones – follicle-stimulating hormone (FSH) and luteinizing hormone (LH) – which are both produced in a small gland – the pituitary gland – situated just beneath the hypothalamus. In young boys, FSH and LH ultimately cause the production of testosterone. If the hypothalamus-pituitary gland pathway is thwarted in any way, the production of the male hormone will be too and puberty will not take on its proper course.

A number of instances can cause hypogonadotropic hypogonadism. Key hormone receptors involved in the pathway can be deficient or missing due to surgery, head trauma or a congenital disease for instance. It was the study of congenital HH which led to the discovery of the KiSS-1 receptor which proved to have a direct role in the proper development of the male and female gonads. The KiSS-1 receptor is found both in the hypothalamus and the pituitary gland and is a G protein-coupled receptor, i.e. it belongs to the very large family of transmembrane receptors whose role is to transduce a signal. Its ligand is the neuropeptide KiSS-1 and together they are involved in the regulation of gonadotropin secretion. As mentioned above, gonadotropin stimulates the production of testosterone in males. Take away the KiSS-1 receptor and Tintin becomes Peter Pan.

Could it be that the famous reporter was indeed inflicted with HH? Perhaps. Could it have been congenital? No one, save his creator Hergé, could answer that. However, what we do know is that the knickerbockered reporter was beaten about the head a fair number of times during his travels around the world. A Canadian team, made up of an Associate Professor with the Faculty of Medicine at the University of Sherbrooke in Quebec and his two young sons, scanned all of Tintin's adventures for blows which had been made to the young man's head, and they discovered that he was subjected to 43 head traumas resulting from such incidents as colliding with tree trunks, falling on ice or receiving a blow from a whisky bottle. The severity of the injuries was judged by the number of candles or stars which revolved above Tintin's head and the number of frames it took him to recover.

Puberty can be arrested following even minor head traumas in children. There may be no loss

of consciousness, no important external injuries or subsequent neurological effects, yet if the stalk which leads from the hypothalamus to the pituitary gland is somehow severed, the natural process of puberty cannot take place because hormonal communication has been lost. So, although Tintin visibly suffered from his injuries and most of them involved loss of consciousness, he didn't need all 43 accidents to acquire HH… A mild blow on his head would have been sufficient.

G protein-coupled receptors are diverse and many. And since they are involved in signalling, the pharmaceutical industry has made great use of them by using them as drug targets. And it has been quite successful. Not only is the KiSS-1 receptor involved in neurological processes – such as the onset of puberty for instance – but its ligand, the KISS-1 peptide was previously shown to prevent metastasis in melanoma cells. Such findings suggest that the KiSS-1 receptor and its ligand may be the bearers of essential roles both in the central nervous system and in tumour biology. And, as a consequence, they could provide valuable targets in the future for novel therapies in the fields of oncology as well as neurology.

Cross-references to Swiss-Prot

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