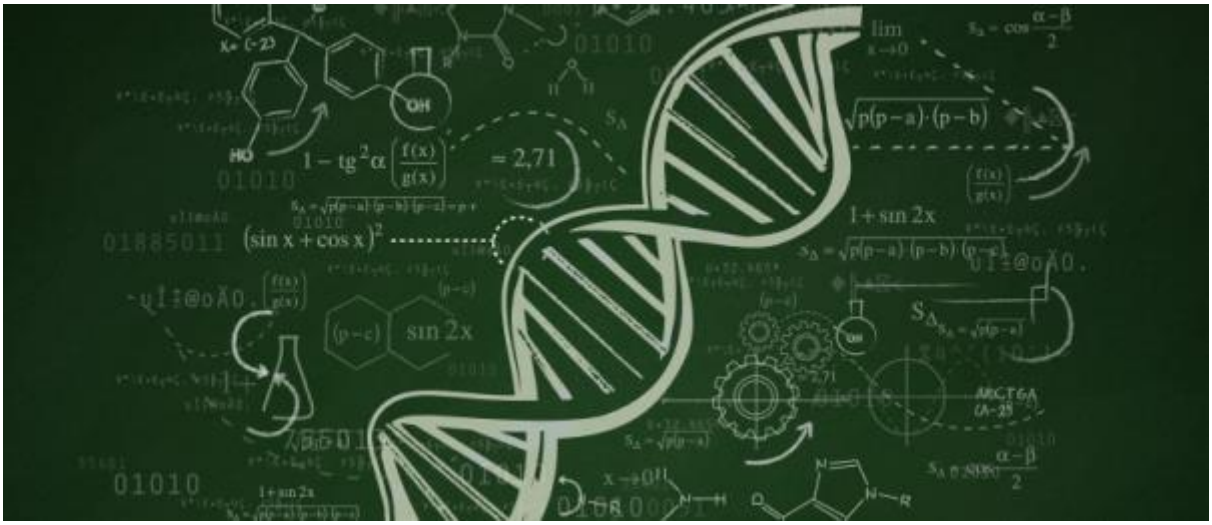
The SMALTIS'tory – episode #4

The first bio-production under hormonal influence.

Once upon a time there was somatostatin, a mammalian hormone that inhibited the secretion of other hormones such as growth hormone, insulin and glucagon.

Well known today for its use in medical imaging and for the treatment of certain pituitary adenomas, somatostatin was the first human protein recombinantly produced in bacteria. Let's go back to this biotechnological innovation published in 1977...

This work carried out by Boyer's team began with the chemical synthesis of the sequence coding for the 14 amino acids of somatostatin. The codons were chosen to promote their expression in *E. coli*, eliminate undesirable pairings and limit transcription termination signals. Then, through a succession of cloning steps in plasmid pRB322, the gene coding for somatostatin was fused to that of β-Galactosidase and placed after the lactose operon. The resulting plasmid named pSomII-3 was then introduced into *E. coli* strain MS2, and transformants were selected using ampicillin and tetracycline. The production of somatostatin was verified by radioimmunoassay. Finally, this work resulted in a strain of *E. coli* able to produce somatostatin protein as a precursor, which was then converted into its functional form by cleavage with cyanogen bromide.

Thus, the synthesis of human somatostatin by *E. coli* marked the first success of bio-production and paved the way for the use of bacteria as peptide factories. Since then, many human proteins used as drugs have been routinely manufactured by bacteria or yeast, such as insulin, which was marketed in 1982.