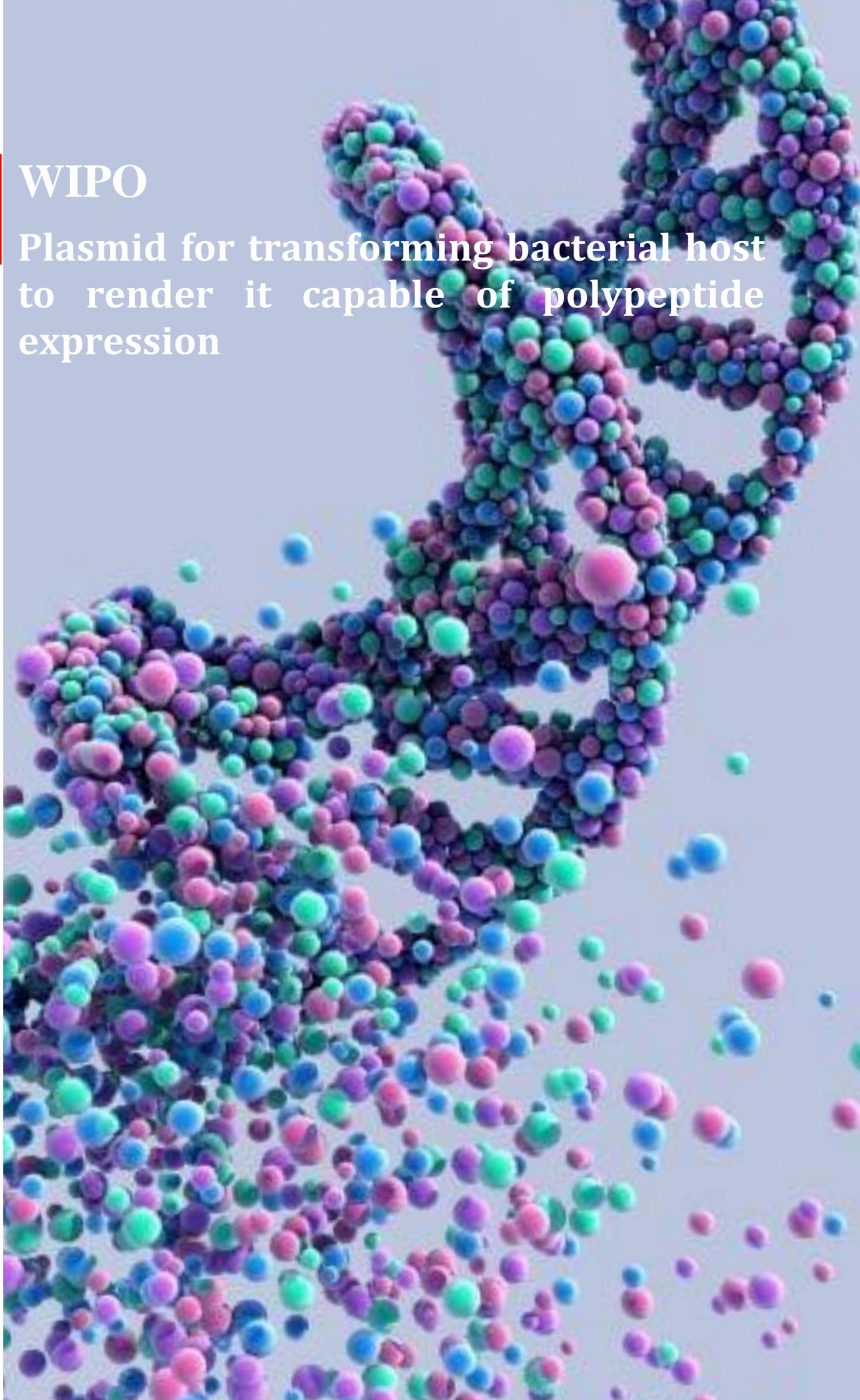


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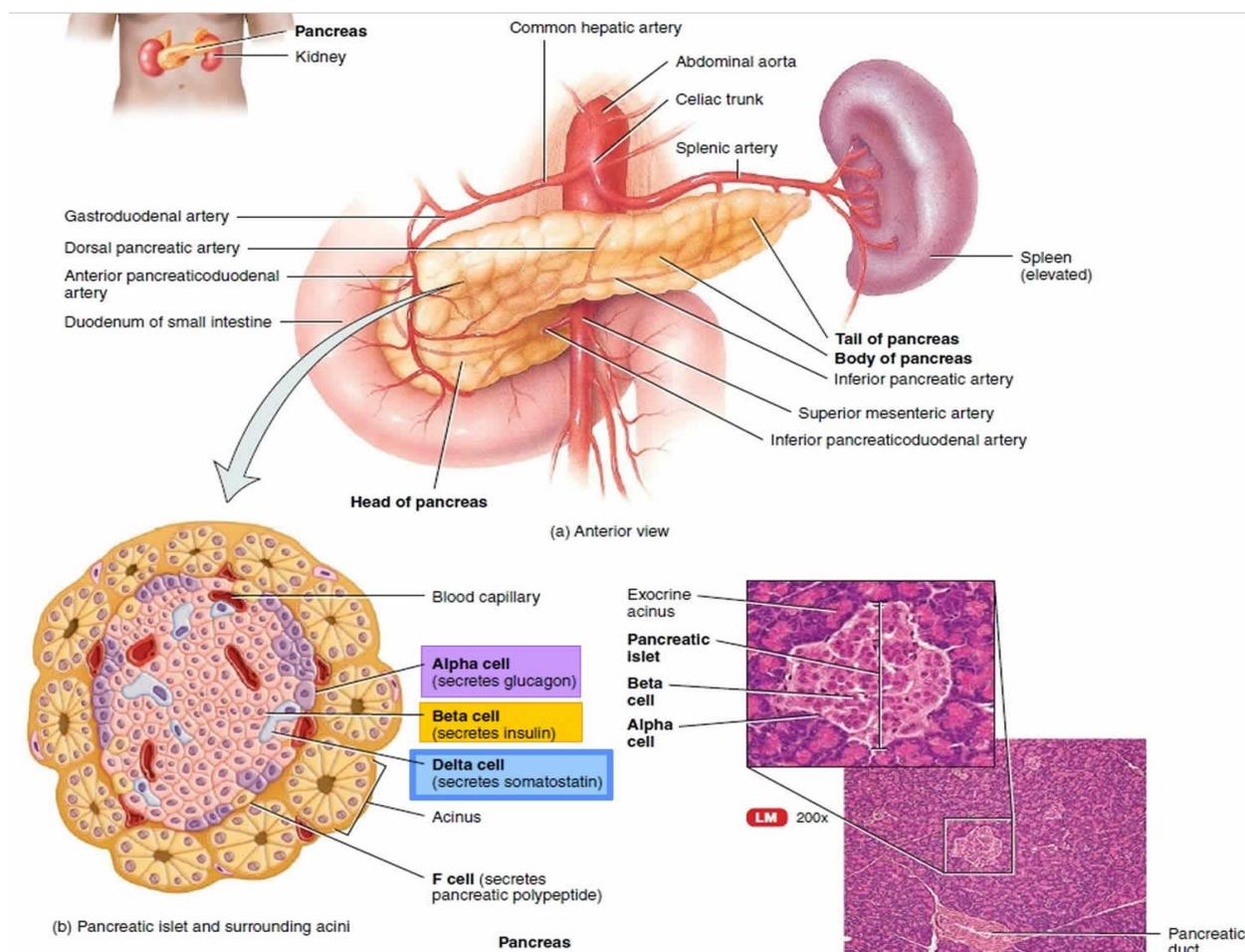
Plasmid for transforming bacterial host  
to render it capable of polypeptide  
expression



## Case Study I – Plasmid for transforming bacterial host to render it capable of polypeptide expression / GENENTECH – Sufficiency of disclosure

Title of the invention	Plasmid for transforming bacterial host to render it capable of polypeptide expression
Assignee/Proprietor	GENENTECH, INC.
The patent	<a href="#">EP0001929A2</a> – pdf file of the patent

### Imagine ©-cleared of Case Study I



**Figure 1** – depicts the production of Somatostatin by the pancreatic islets of delta cells of the [islets of Langerhans](#). Source - HealthJade.net: <https://healthjade.net/somatostatin/>

### Abstract of Case Study I

In this case, we will look at an important European Patent ([EP0001929B1](#)) for an invention related to “Plasmid for transforming bacterial host to render it capable of polypeptide expression” filed on November 6<sup>th</sup> 1978 by Genentech, Inc. and with Keiichi Itakura *et al.* as the inventor. This Patent had a chequered path leading to a final revocation by the EPO Technical Board of Appeal on September 17<sup>th</sup>, 1998. The patent application of Itakura *et al.* was initially refused by the EPO Examining Division but subsequently granted on appeal ([T292/85](#)) by the EPO Technical Board of Appeal on January 27<sup>th</sup> 1988, albeit with amended claims. Thereafter, following opposition proceedings, wherein the claims were further amended, the EPO Opposition Division revoked the patent and this decision was upheld on appeal ([T0794/94](#)) by the EPO Technical Board of Appeal, leading to a final revocation on 17<sup>th</sup> September 1998 for lack of enabling disclosure.

## Case Study I – A patent application for a genetic resources-related invention which has sufficiency of disclosure

The patent of Itakura *et al.* was directed to the recombinant plasmids comprising heterologous DNA coding for the expression of mammalian hormones (e.g., somatostatin) and other polypeptides, and process for preparing the recombinant plasmids. The patent also discloses the use of the recombinant plasmid for use in the transformation of a bacterial host to render said host capable of expressing the hormone somatostatin.

Somatostatin exists in two forms: one composed of 14 [amino acids](#) and a second composed of 28 amino acids. Somatostatin is also known as a growth-hormone-inhibiting hormone, and inhibits hormones released from the anterior pituitary gland and gastrointestinal system as well as the pancreas. In the [pancreas](#), somatostatin is produced by the delta cells of the [islets of Langerhans](#). Somatostatin inhibits [insulin](#) and [glucagon](#) release from [adjacent](#) cells in the pancreas. Insulin, glucagon, and somatostatin act in concert to control the flow of nutrients into and out of the [circulation](#).<sup>1</sup>

The granted Claim 1 is directed to:

A recombinant plasmid suitable for transformation of a bacterial host wherein the plasmid comprises a heterologous DNA encoding a desired functional polypeptide or intermediate thereof which is not degraded by endogenous proteolytic enzymes. The heterologous DNA is positioned in proper reading frame whereby the resulting expression product is a functional polypeptide or intermediate thereof.

In its decision dated May 15<sup>th</sup> 1985 and notified on July 23<sup>rd</sup> 1985, the EPO Examining Division refused the grant of claims 1 to 12 of the patent application of Itakura *et al.* on the grounds of lack of sufficient disclosure (Article 83 EPC) and lack of inventive step (Article 56 EPC).

Aggrieved by this refusal, the patent applicant approached the EPO Technical Board of Appeal, challenging the decision of the EPO Examining Division. The EPO Technical Board of Appeal by its order ([T292/85](#)) dated January 27<sup>th</sup> 1988 allowed the appeal and set aside the decision of the EPO Examining Division and allowed the grant of the patent with amended set of claims 1 to 16 of patent application of Itakura *et al.* filed before the Board. In this order the EPO Technical Board of Appeal notably held that an invention is sufficiently disclosed if at least one way is clearly indicated enabling the person skilled in the art to carry out the invention. The Board also held that the unsuitability of some unspecified particular variants of a functionally defined component feature of the invention is immaterial to sufficiency as long as there are suitable variants known to the skilled person through the disclosure or common general knowledge which provide the same effect for the invention.

It was further held that generally applicable biological processes are not insufficiently described for the sole reason that some starting materials or genetic precursors are not readily available to obtain each and every variant of the expected result of the invention, provided the process as such is reproducible.

Following the above decision of grant by the EPO Technical Board of Appeal, notices of opposition were filed by seven opponents seeking the revocation of the patent of Itakura *et al.* on the grounds of lack of sufficient disclosure and lack of inventive step, amongst others. The EPO Opposition Division also considered the amended claims put forth by the applicant of the patent of Itakura *et al.* and in its order dated July 22<sup>nd</sup> 1994 revoked the patent for lack of inventive step.

Aggrieved by this decision, an appeal ([T0794/94](#)) was filed by the applicant of the patent of Itakura *et al.* before the EPO Technical Board of Appeal and the amended set of claims 1 to 6 were asserted before the Board in the appeal proceedings.

Claim 1 of the patent of Itakura *et al.* in the appeal proceedings were directed to a plasmid suited for direct expression of a desired functional mammalian polypeptide or intermediate therefor which is not degraded by endogenous proteolytic enzymes. The Board observed that there is no example in the specification of direct expression of mammalian proteins.

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<sup>1</sup> <https://www.britannica.com/science/somatostatin>

The Board thus held that it is unable to formulate any problem in relation to claim 1 of the patent of Itakura *et al.*, for which it can be said that it has been solved by the novel information. The Board also held that it cannot be said that the actual contribution to the state of the art made by the disclosure of the patent of Itakura *et al.* consists of providing experimental support for the direct expression of mammalian proteins, i.e., the technical contribution is not a new technique, but the successful completion of an experiment known at a theoretical level from the prior art. This is because the direct expression of mammalian proteins is not exemplified in the patent in suit. Therefore, the Board held that either the skilled person could make what is claimed in claim 1 of the patent of Itakura *et al.* already on the basis of the prior art, or both the prior art and the patent of Itakura *et al.* contain insufficient information to realize what is claimed in claim 1 of the patent of Itakura *et al.* Thus, the Board held that claim 1 of the patent of Itakura *et al.* must fail as the requirements of sufficient disclosure and demonstration of inventive step have not been fulfilled and accordingly dismissed the appeal and upheld the revocation of the Itakura *et al.* patent.