DLC-427 Intellectual Property and Genetic Resources in the Life Science

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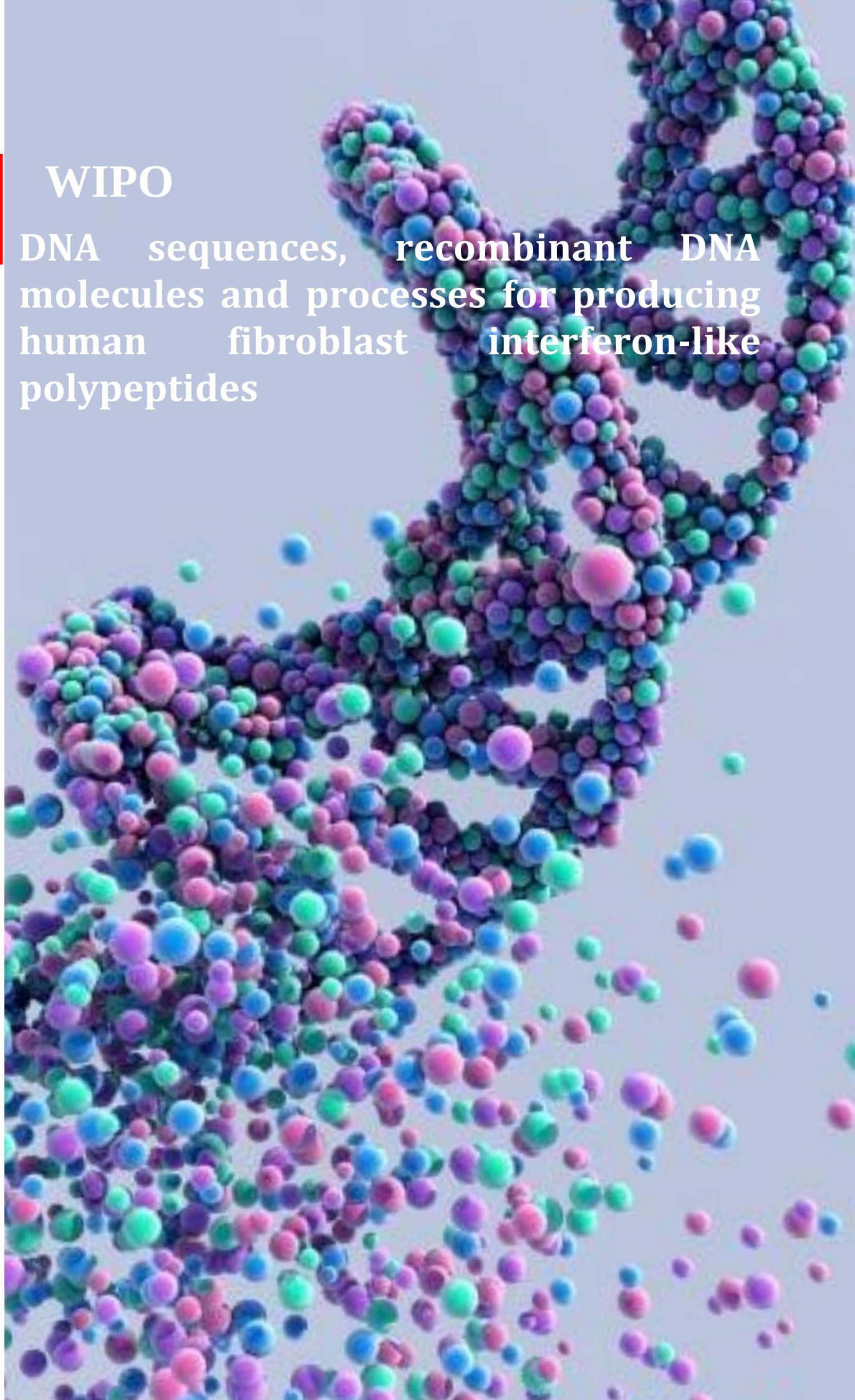
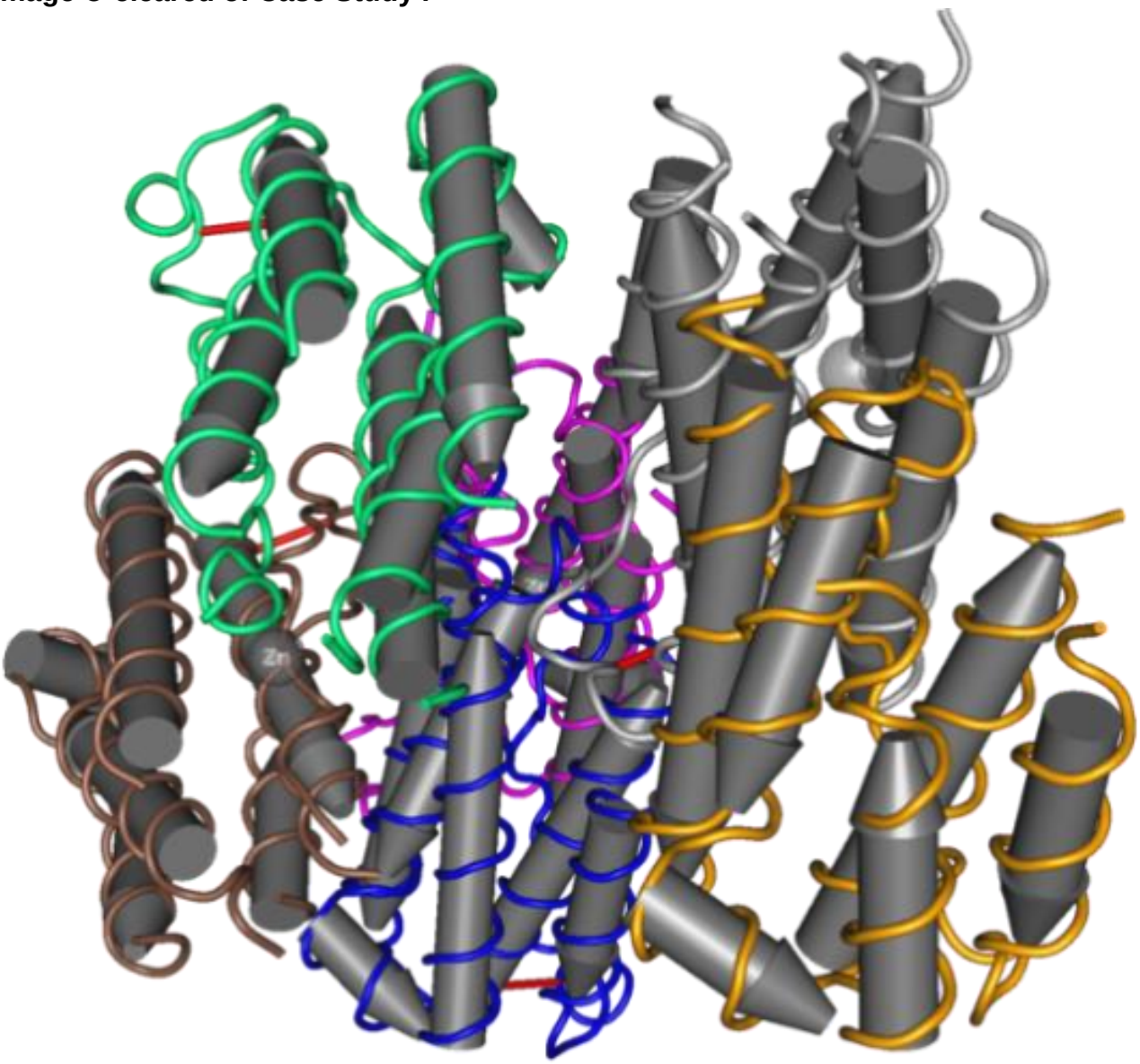
DNA sequences, recombinant DNA molecules and processes for producing human fibroblast interferon-like polypeptides



Case Study F – DNA sequences, recombinant DNA molecules and processes for producing human fibroblast interferon-like polypeptides / BIOGEN – *The meaning of reasonable expectation of success*

Title of the invention	DNA sequences, recombinant DNA molecules and processes for producing human fibroblast interferon-like polypeptides
Assignee/Proprietor	**BIOGEN, INC.**
The patent	EP0041313A2 – pdf file of the European Patent Application EP0041313B1 – pdf file of the European Patent Specificaiton

Image ©-cleared of Case Study F



1RH2 Recombinant Human Interferon Alpha 2b (2002)

Abstract of Case Study F

In this case study we will look at an important European Patent directed to *"DNA sequences, recombinant DNA molecules and processes for producing human fibroblast interferon"* filed on April 1, 1981, by Biogen Inc., with Dr. Charles Walter Fiers as the inventor, and granted on September 12, 1990. The said patent was

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revoked following opposition proceedings by the EPO Technical Board of Appeal on April 8, 1997. The patent illustrates an example of a GR-based invention which lacks inventive step in the meaning of patent law.

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Case Study F – A genetic resources-related invention which lacks an inventive step

The patent of Dr. Charles relates to DNA sequences, recombinant DNA molecules and process for producing human fibroblast interferon-like polypeptides. More particularly, the invention relates to DNA sequences expressed in an appropriate host organism. The recombinant DNA molecules disclosed therein are characterized by DNA sequences that code for polypeptides whose amino acid sequence and composition are substantially consistent with human fibroblast interferon and which have an immunological or biological activity of human fibroblast interferon. The DNA sequences, recombinant DNA molecules and processes of the said invention could be used in the production of polypeptides useful in antiviral and antitumor or anticancer agents and methods.

Pursuant to the grant of the patent (EP0041313B1), a notice of opposition was filed challenging the grant of the patent of Dr. Charles on the grounds of lack of lack of novelty and inventive step and also on the ground of insufficiency of disclosure.

In its decision dated January 21, 1994, the EPO Opposition Division rejected the opposition and maintained the grant of the patent of Dr. Charles. The EPO Opposition Division considered that sufficient information was given in the patent specification on how to test the interferon (IFN) biological and immunological activities and on how to isolate and identify the variants. The EPO Opposition Division also held that novelty was acknowledged over the cited prior art documents as those documents did not provide convincing evidence that the plasmid they disclosed could have expressed IFN-beta from any of the pBR322 promoters. The EPO Opposition Division also held that the experimental data submitted by the opponent did not credibly show that the anti-viral activity seen in hosts containing said plasmid was due to the expression of the human IFN-beta gene. On this ground of lack of inventive step, the EPO Opposition Division observed that the technical problem to be solved by the patent of Dr. Charles was the recombinant production of a polypeptide displaying the immunological or biological activity of human IFN-beta. Accordingly, it was held that human IFN-beta could not have been expressed in a straightforward manner by the then existing methods of expression. Furthermore, the EPO Opposition Division held that in view of the physical and chemical differences between IFN-beta and the mammalian proteins which had already been produced in recombinant form, successful expression could not have been predicted and therefore acknowledged inventive step.

Aggrieved by the order of the EPO Opposition Division, the opponent approached the EPO Technical Board of Appeal, challenging the order of the EPO Opposition Division.

The EPO Technical Board of Appeal reversed the decision of the EPO Opposition Division and revoked the patent of Dr. Charles. While assessing the novelty of the patent of Dr. Charles, the Technical Board of Appeal considered prior art documents that disclose a plasmid TpIF319-13 which carries the beta-IFN cDNA in the EcoRI site of pBR322 in such an orientation that it could theoretically be transcribed from the P4 promoter of pBR322 and noted that if this is so in practice, the said documents could be novelty-destroying for the subject-matter of claim 1 of the patent of Dr. Charles. The EPO Technical Board of Appeal noted EPO precedents that the teachings of a document belonging to the prior art must be unambiguous before they can be taken into account for assessing novelty and held that none of the cited prior art documents destroy the novelty of the subject-matter of claim 1 of the patent of Dr. Charles. The novelty was also acknowledged for the remaining claims of the patent of Dr. Charles.

On the ground of lack of inventive step, the EPO Technical Board of Appeal considered one of the prior art documents asserted to be the closest prior art document which discloses the cloning of beta-IFN cDNA as well as its sequence. The Board considered that starting from this prior art, the objective technical problem to be solved is the recombinant production of a polypeptide displaying immunological or biological activity of human beta-IFN. The Board further held that considering that the need for beta-IFN was clearly expressed in

the prior art and that recombinant DNA technology was generally regarded as the means to produce a hitherto rare protein and known to a person skilled in the art, the formulation of the problem in the patent of Dr. Charles, is obvious.

The Board reasoned and analyzed that the construction of the beta-IFN expression vector *per se*, using promoter systems known to work in the prior art should not require more than routine work from the average skilled person. The Board thus considered that the central issue to be decided is whether the skilled person would have reasonably expected the beta-IFN cDNA to be expressed in the recombinant host as an active protein, in the light of the known properties of the human beta-IFN. In this context, the Board held that it has to be borne in mind that "the hope to succeed" should not be misconstrued as "a reasonable expectation of success. The Board held that the former is the mere expression of a wish whereas the latter requires a scientific evaluation of the facts at hand. In the case of gene expression, the Board held that this evaluation necessitates that the properties of the "expression partners" (the gene to be expressed and its protein product on the one hand, and the recombinant host on the other) be compared. The Board thus held that the skilled person would consider the knowledge of the properties of beta-IFN as an asset in identifying in the light of the state of the art which problems, if any, such properties may cause, and which solutions were available. By doing so, the skilled person would come to the conclusion that the properties of beta-IFN were not such as to bar the way to its expression. Accordingly, the EPO Technical Board of Appeal held that the patent of Dr. Charles did not demonstrate inventive step and was thus liable to be revoked

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