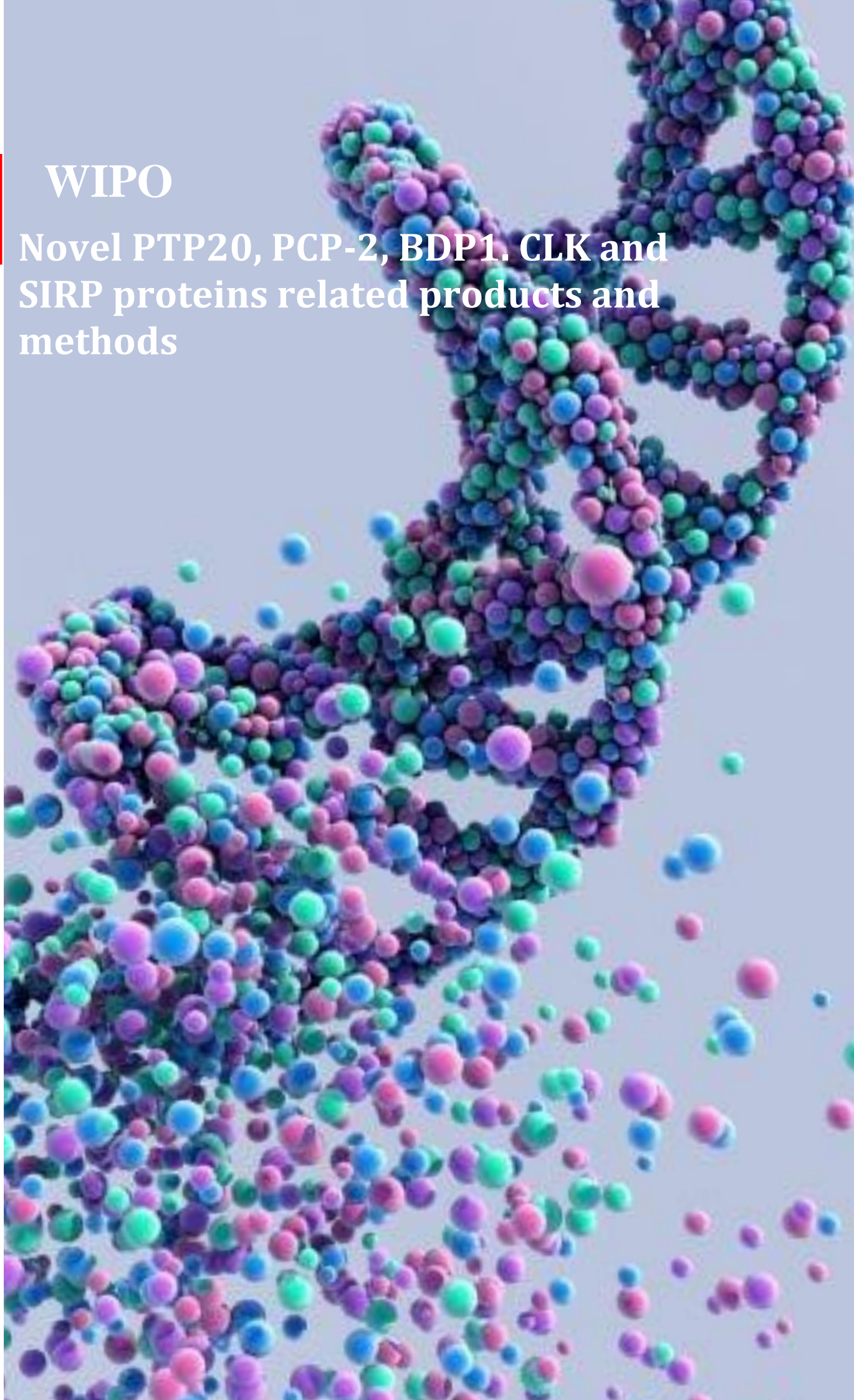


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Novel PTP20, PCP-2, BDP1, CLK and
SIRP proteins related products and
methods



Case Study G – Novel PTP20, PCP-2, BDP1, CLK and SIRP proteins related products and methods / MAX PLANCK INSTITUTE – Importance of Industrial Applicability

Title of the invention	Novel PTP20 ¹ , PCP-2 ² , BDP1 ³ , CLK ⁴ and SIRP ⁵ proteins related products and methods
Assignee/Proprietor	MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN, E.V.
The patent	WO199709748723A2 – pdf file of the International Application Published under the Patent Cooperation Treaty (PCT)

Abstract of Case Study G

In this case study we will look at an important European Patent Application directed to “*Novel PTP20, PCP-2, BDP1, CLK and SIRP Proteins and Related Products and Methods*” filed on 17th June 1997 by Max-Planck-Gesellschaft zur Förderung der Wissenschaften e.V. and with Axel Ullrich et al. as the inventors and was refused by the EPO Examining Division and also by the EPO Technical Board of Appeal on appeal on 11th May, 2005.

Case Study G – A genetic resources-related invention which lacks industrial applicability/utility

Axel’s patent application relates to nucleic acid molecules encoding full length PTP20, PCP-2, BDP1, mCLK2, mCLK3, mCLK4, and SIRP polypeptides, portions of such nucleic acid molecules, nucleic acid vectors containing such nucleic acid molecules, recombinant cells containing such nucleic acid vectors, polypeptides purified from such recombinant cells, antibodies to such polypeptides, and methods of identifying compounds that bind such polypeptides or abrogate their interactions with natural binding partners. It also pertains to methods for diagnosing abnormal conditions in an organism with PTP20, PCP-2, BDP1, mCLK2, mCLK3, mCLK4, and SIRP related molecules or compounds as well as methods for treatment, diagnosis, and screening for diseases related to PTP20, PCP-2, BDP1, mCLK2, mCLK3, mCLK4, and SIRP polypeptides or conditions characterized by an abnormal interaction between such a polypeptide and its binding partner.

Axel’s patent application related to the general field of phosphatases, in particular protein tyrosine phosphatases (PTPases), and among them it was concerned with the specific non-transmembrane (cytosolic) PTPase BDP1 (“Brain Derived Phosphatase 1”). PTPases and tyrosine kinases (TKs) were known in the prior art to be involved in cellular signal transduction pathways. At the priority date of Axel’s patent application, the compounds involved in these signal cascade pathways were not yet fully characterized. Scientific studies were carried out to determine them and to elucidate a complete signal transduction pathway. In this context, progress in the understanding of the function and role of the TKs (and the resulting phosphorylation events) in cellular pathways was extensive, including the identification of several TKs in tumor cell growth (cancer), such as the TK activity of the EGF receptor HER2 in colon cancer. However, the situation was different for the PTPases which were considered to have a more general function by affecting only in a non-specific and indirect manner the effects of these TKs. The technical contribution of the Axel’s patent application was required to be assessed in the context of this general prior art. Since there was a very limited number of available PTPases, in particular non-transmembrane PTPases, having a well characterized biological function, it was emphasized that the disclosure of a biological role for these enzymes represented an important technical contribution to this prior art.

¹ PTP20 – Protein Tyrosine Phosphatases 20

² PCP-2 – Pancreatic Carcinoma Phosphatase 2

³ BDP1 – Brain Derived Phosphatase 1

⁴ CLK – Cdc-Like Kinase (Cdc – Cell division control)

⁵ SIRP – Signal Regulatory Proteins

Axel's patent application disclosed the molecular characterization of a newly identified PTPase (BDP1) and revealed specific features that enabled the elucidation of its cellular function. BDP1 was shown to belong to the PTPase-PEST family of PTPases, a family characterized by the occurrence of PEST sequences (rich in Pro, Glu/Asp, and Ser/Thr) which were believed to provide a mechanism for rapid cellular turnover. The experimental results disclosed in Axel's patent application clearly suggested and identified a role of BDP1 in cancer, namely a tumor-suppressor activity in several specific cancers. Therefore, it was asserted that the non-transmembrane PTPase BDP1 was made readily available to the skilled person as a suitable target for therapy intervention and a promising drug-candidate. Based on this disclosure, it was asserted that the skilled person was put in a position to perform normal and/or standard pharmaceutical-clinical studies that, depending on their outcome, would lead to the development and optimization of the most suitable pharmaceutical compositions.

In its decision dated 19th February 2004, the EPO Examining Division refused grant of Axel's patent application pursuant to objections in relation to added subject-matter (Article 123(2) EPC), lack of support (Article 84 EPC), insufficient disclosure (Article 83 EPC), lack of novelty (Article 54(3)(4) EPC), lack of inventive step (Article 56 EPC) and lack of industrial application (Article 57 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 dismissed the appeal and upheld the refusal of Axel's patent application.

The EPO Technical Board of Appeal referred to and considered Article 52(1) EPC, which stated that for a European patent to be granted an invention has to satisfy *inter alia* the requirement of being "susceptible of industrial application". According to Article 57 EPC, this requirement is fulfilled if the invention "can be made or used in any kind of industry, including agriculture". In this respect, Rule 27(1)(f) EPC prescribes that the description should "indicate explicitly, when it is not obvious from the description or nature of the invention, the way in which the invention is capable of exploitation in industry." Rule 23e(3) EPC, which is in relation to biotechnological inventions, similarly requires that "the industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application".

The Board also referred to precedents and noted that the case law indicates that the notion of "industry" has to be interpreted broadly to include all manufacturing, extracting and processing activities of enterprises that are carried out continuously, independently and for financial gains. The Board thus observed that the requirement of Article 57 EPC that the invention "can be made or used" in at least one field of industrial activity emphasizes that a "practical" application of the invention has to be disclosed. The Board also noted that merely because a substance (in the instant case of Axel's patent application being a polypeptide) could be produced in some ways does not necessarily mean that this requirement is fulfilled, unless there is also some profitable use for which the substance can be employed.

The Board also observed that in cases where a substance, naturally occurring in the human body, is identified, and possibly also structurally characterized and made available through some method, but either its function is not known or it is complex and incompletely understood, and no disease or condition has yet been identified as being attributable to an excess or deficiency of the substance, and no other practical use is suggested for the substance, then industrial applicability cannot be acknowledged. The Board pertinently noted that while the jurisprudence has tended to be generous to applicants, there must be a borderline between what can be accepted, and what can only be categorized as an interesting research result which *per se* does not yet allow a practical industrial application to be identified. The Board held that even though research results may be a scientific achievement of considerable merit, they are not necessarily an invention which can be applied industrially.

Applying the above principles to Axel's patent application, the Board analyzed that in the present case, while the claimed BDP1 polypeptide is described as a substance found in the human body and as having unique properties, the question that arises for consideration is whether any disclosure or suggestion has been made as to how these properties of BDP1 might be exploited.

In this regard, the Board observed that Axel's patent application does not explicitly disclose the specific nature and the possible significance of the suggested roles for BDP1. The Board noted that Axel's patent application stops short of suggesting, let alone identifying, an anti-cancer activity for BDP1 or a therapeutic use of BDP1 as a tumor-suppressor agent. The board considered that there is no evidence as to whether BDP1 plays a passive role (as by-product of certain cancerous processes only) or an active role in cancer and whether, in the latter case, the said role is a positive (promoting and/or supporting tumor growth and/or differentiation) or a negative (tumor-suppressor) one. Moreover, the Board noted that taking into account the fact that both cancer and cellular housekeeping are complex cellular processes which involve a large number of genes and/or proteins with multiple specific interconnections and finely tuned regulations (reflecting the complexity of the cellular signal transduction pathways), the nature and significance of these roles cannot be inferred from Axel's patent application itself since the over-expression/under-expression of a single signal (BDP1) may not result in a simple effect but in multiple and unexpected ones (alteration of housekeeping system) within these complex and finely regulated cellular pathways, i.e. the modulation or alteration of one single signal (BDP1) does not take place in a simple black-or-white manner but in a complex network of interconnected pathways.

The Board considered the documentary evidence adduced by the patent applicant and noted that although it is shown that BDP1 down-regulates the phosphorylation of HER2 protein itself as well as downstream signaling events, how this is accomplished by BDP1 remains elusive. The Board held that while there is no doubt that a BDP1 polypeptide could be "made and used" as a further tool, in addition to the many already available in the art for exploring the complex cellular signal transduction pathways and their implications in the regulation of cellular processes and, possibly, disease states; however, acknowledged that the whole burden is left to the reader to guess or find a way to exploit it in industry by carrying out work in search for some practical application geared to financial gain, without any confidence that any practical application exists.

The Board thus held that although Axel's patent application describes a product (a polypeptide), means and methods for making it, and its prospective use thereof for basic science activities, it identifies no practical way of exploiting it in at least one field of industrial activity. The Board considered this to be a vague and speculative indication of possible objectives that might or might not be achievable by carrying out further research with the tool as described is not sufficient for fulfilment of the requirement of industrial applicability and observed that the purpose of granting a patent is not to reserve an unexplored field of research for an applicant. It was thus held that Axel's patent application lacked industrial applicability and thus could not proceed to grant.

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⁶ *Supra* Note 20.