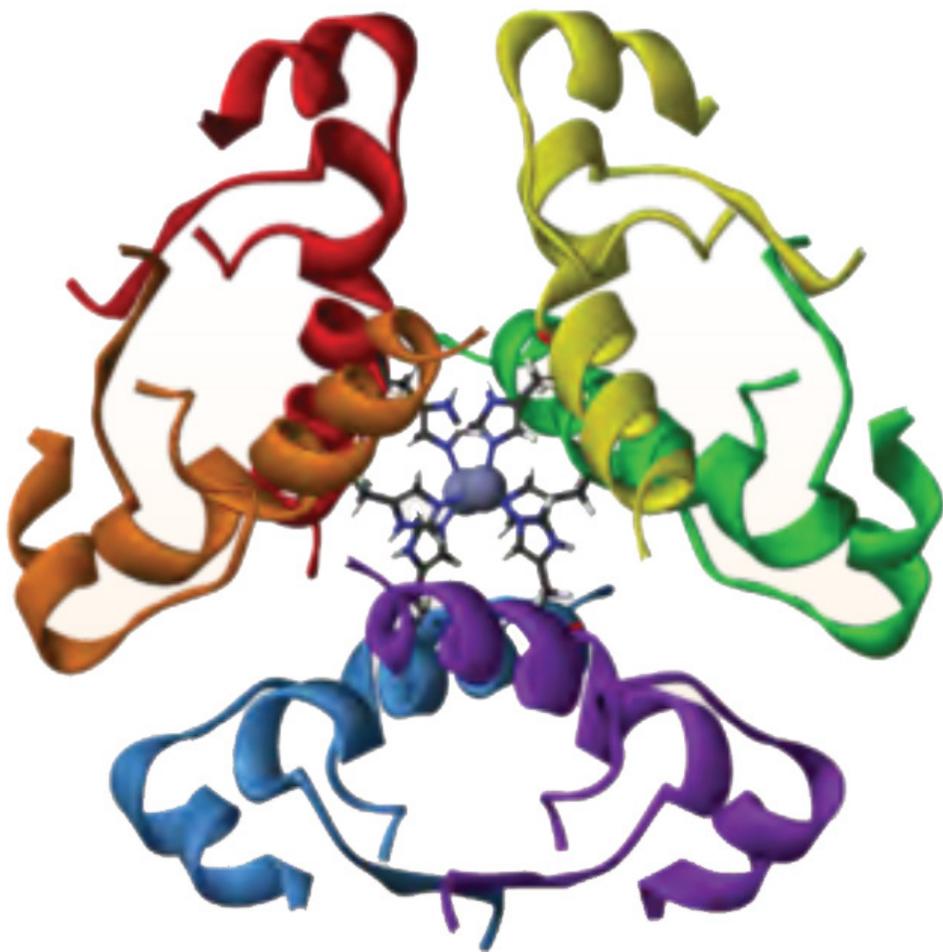




Cytofold StructQuant[®] Protein Folding Technology



Paras Biopharmaceuticals Finland Oy
(Microbial Biologics CDMO, Biosimilars & Bioprocess Enzymes)

Cytofold StructQuant® Technology- Unique Cytoplasmic Oxidative Protein Folding

Paras Cytoplasmic Oxidative Protein Folding

Cytofold StructQuant® is a propriety technology of Paras Biopharmaceuticals, for the high level expression of homogeneously folded disulfide bond containing proteins in the cytoplasm of *E. coli*. The technology offers all of the cost benefits of expression in *E. coli* rather than in eukaryotic systems, while at the same time retaining the high yields obtained in cytoplasmic expression. The biologics produced are of the highest quality and have maximal biological activity.

Advantages of Cytofold® Technology

Cytofold StructQuant® technology allows:

- Low cost production of biologics that contain disulfide bonds
- Large scale production of biologically active eukaryotic proteins in the cytoplasm of *E. coli*.
 - Decreased production costs via high yield production in *E. coli*
- Reduced process development time as in vitro refolding optimization is not required.

Protein Folding Technologies

Disulfide bond formation is a post-translational modification that is required for the correct folding and function of around one-third of human proteins, including most secreted and outer-membrane proteins. Proteins that include disulfide bonds include: insulin, antibody fragments, interleukins, interferons, erythropoietin and many others.

Native disulfide formation is a complex multi-factorial process and has not been possible in the cytoplasm of *E. coli* due to the presence of two reducing pathways. The synthesis of disulfide bond containing proteins is therefore either done in eukaryotic cells, in the periplasm of bacteria or by using in vitro oxidative refolding methods. All of these have problems relating to cost and efficiency.

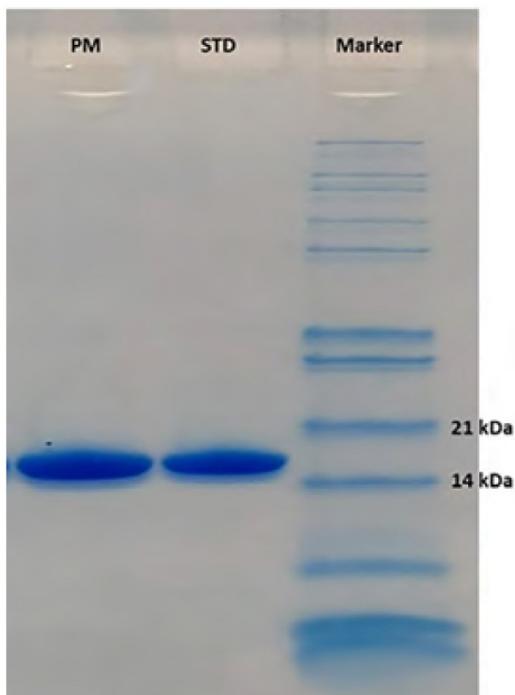
New Technology Developments

Unlike previous systems, this works in any *E. coli* strain and does not require the disruption of the reducing pathways naturally present. The system also works in all media and does not require any supplementation of the media, reducing costs.

The system has been successful for the production in yields up to 1gm/L from shake flasks and in excess of 4 - 6gm/L in fermentation.



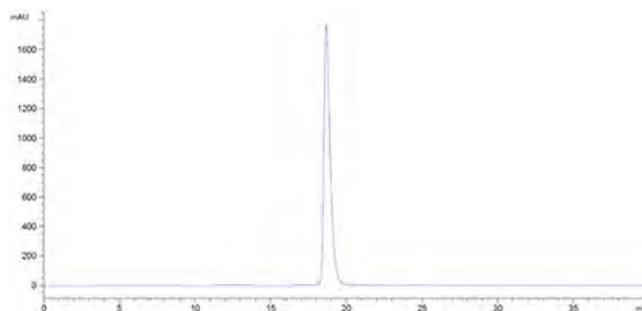
High Level Protein Production



Production of Paras Product 1 in yields of more than 5 gm/L of purified protein from fermentation. Paras Biopharmaceuticals is currently combining this Cytofold StructQuant® technology with Paras Biomultifold® to further increase yields.

The proteins produced are homogeneously folded, have native disulfide bonds and full biological activity. By avoiding time-consuming and inefficient in vitro refolding, the use of CytofoldStruct Quant® significantly reduces production costs and development time.

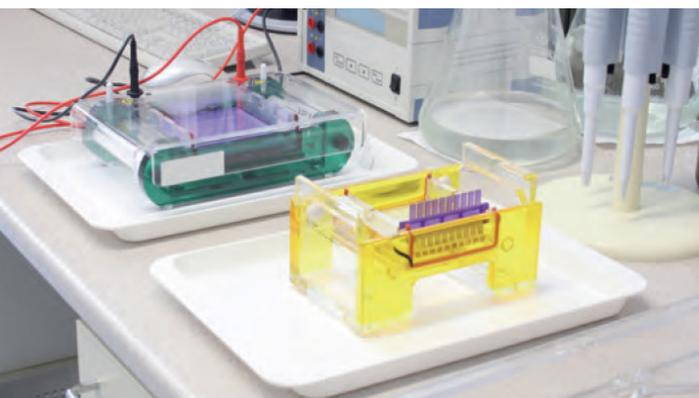
Product Validation with HPLC

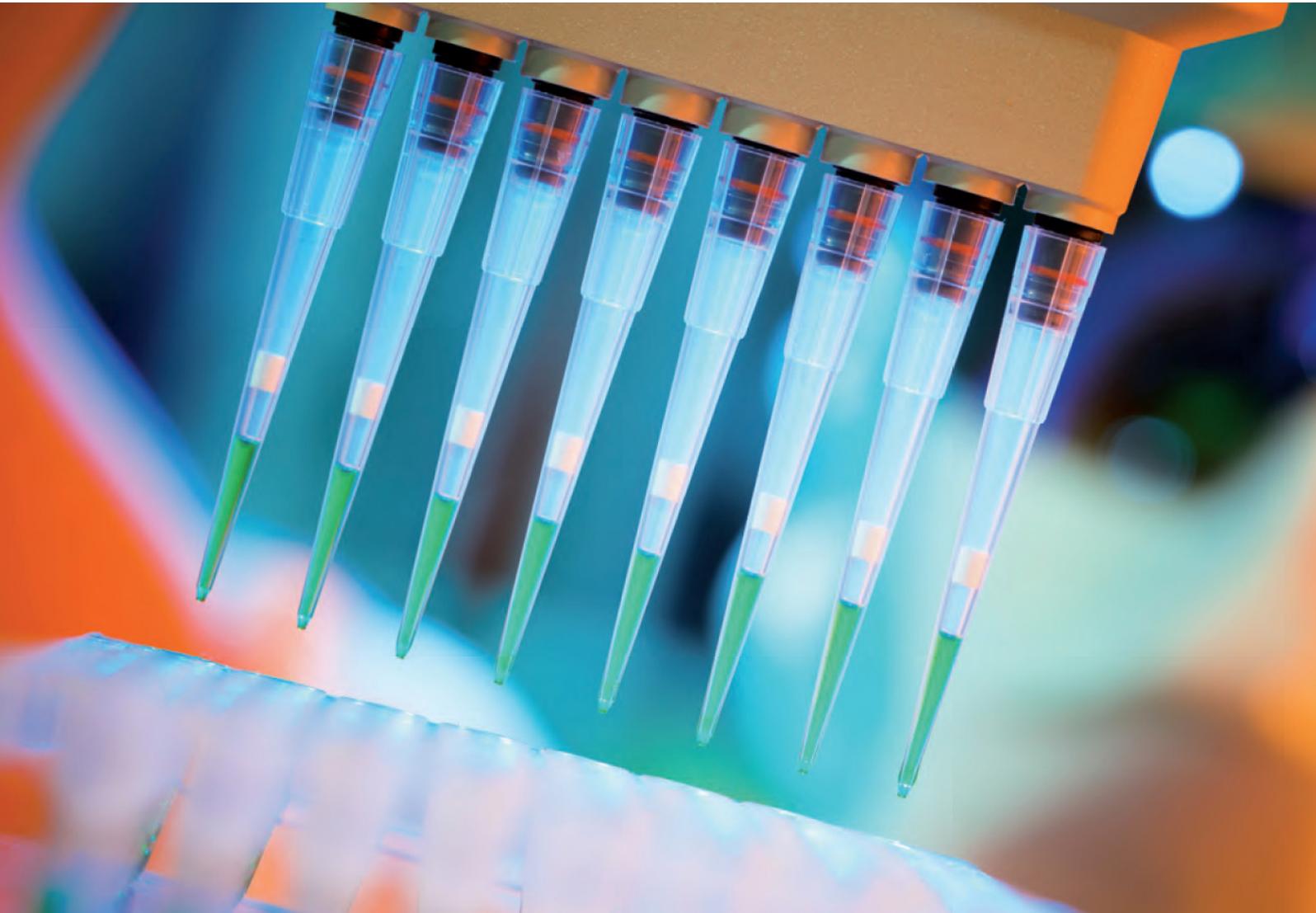


HPLC Chromatogram showing Product Elution at Appropriate RT.

Expertise at Paras Biopharmaceuticals

Paras Biopharmaceuticals Finland can make full use Cytofold StructQuant® for the development of its own products and in the development of production processes for other companies. Furthermore, Paras Biopharmaceuticals Finland Oy has in-house expertise in Cytofold StructQuant® technology to ensure that the most appropriate variant is used to further cut the cost and time of development.





For more details, write us to

Paras Biopharmaceuticals Finland Oy
Kiviharjunlenkki 10
90220 OULU, FINLAND

www.parasbiopharma.com
BD@parasbiopharma.com

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