Bioprocess Design for Human Hemoglobin Production in *Saccharomyces cerevisiae* – Part I: Process Strategy

Bachelor's Degree Final Project – Biotechnology
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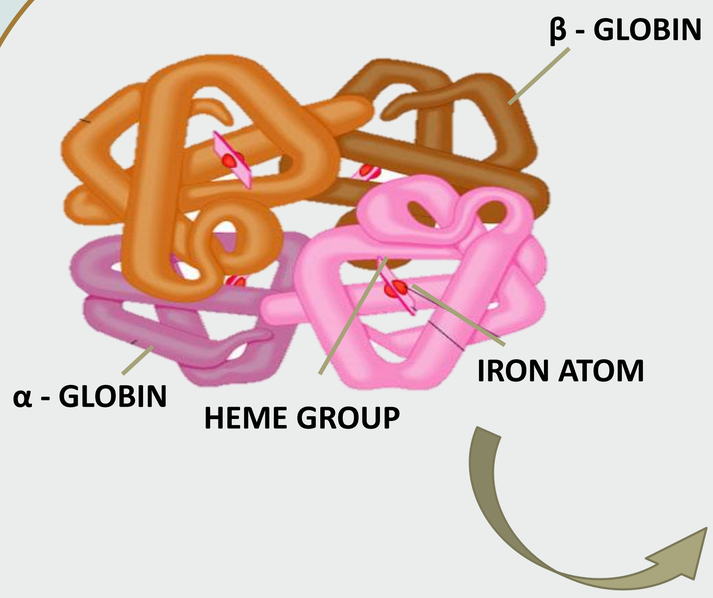
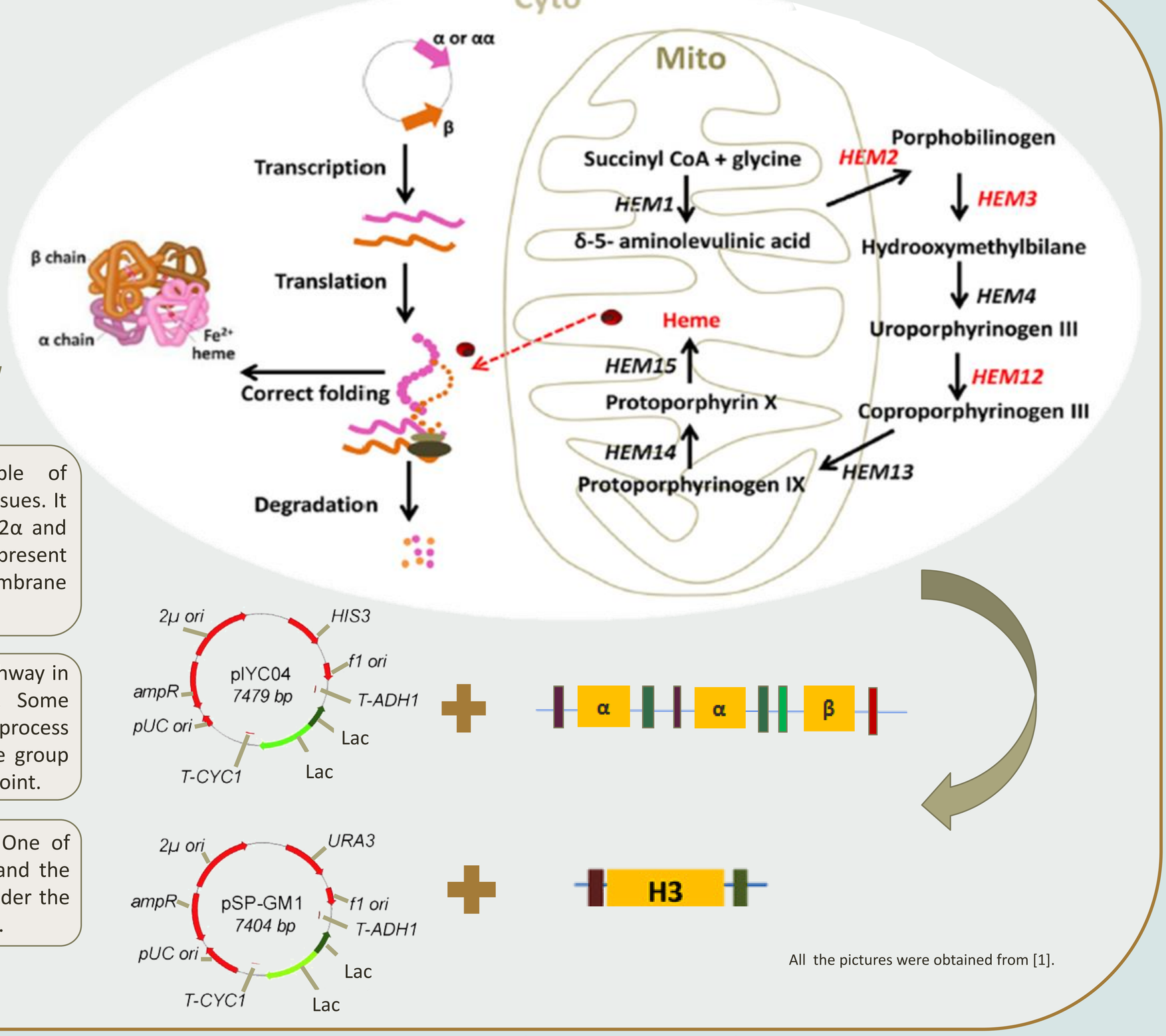
INTRODUCTION

It is expected that within 30 years, the progressive aging of the population will make blood donations decrease dramatically. Therefore, this project is born with the objective of solving part of this severe problem through human hemoglobin production in *Saccharomyces cerevisiae* and its application to industrial scale. The molecule will be encapsulated in a liposome in order to simulate an erythrocyte, a system that allows us to ensure the stability of the protein when administered. Due to the lack of surface antigens, this method will not produce histocompatibility problems. Thus, it is possible to reach the main goal of the work: to save lives and to improve people's health.

METABOLIC PATHWAY AND GENETIC ENGINEERING





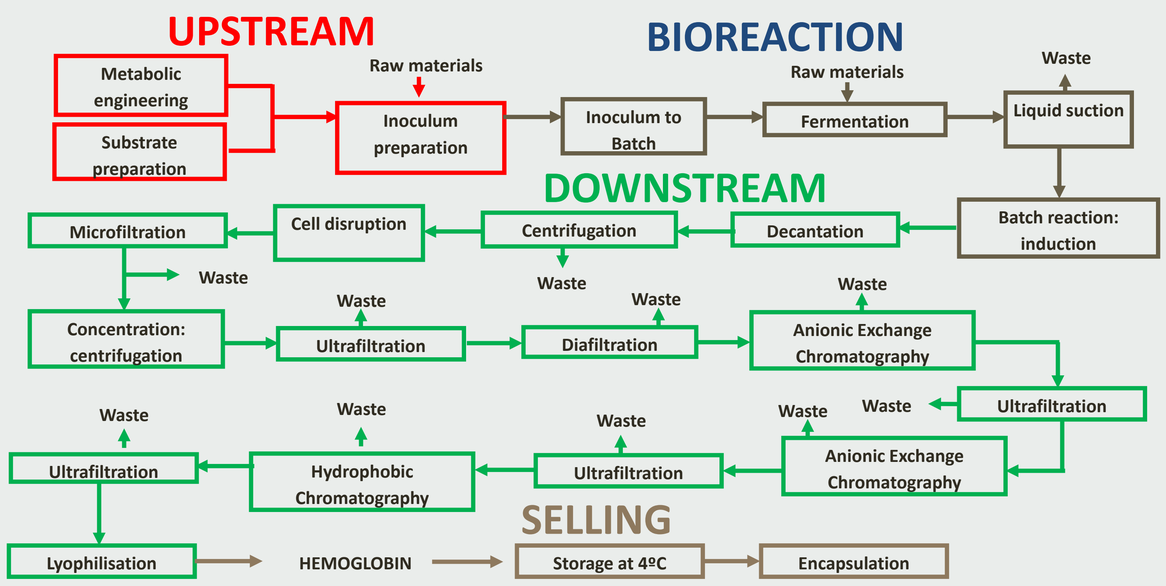
1 Hemoglobin is the protein responsible of transporting the oxygen to the different tissues. It is composed of four polypeptidic chains, 2α and 2β, joined each one to a heme group. It is present in blood and covered in a plasmatic membrane forming the erythrocytes.

2 It is possible to simulate the metabolic pathway in *Saccharomyces cerevisiae* to produce it. Some studies reported that the bottleneck of the process is the HEM3 enzyme, related to the heme group synthesis. Overpassing this barrier is a key point.

3 A combination of two plasmids is used. One of them overexpresses the α and β globins and the other one, the HEM3 enzyme. Both are under the control of the lac operon, which is inducible.

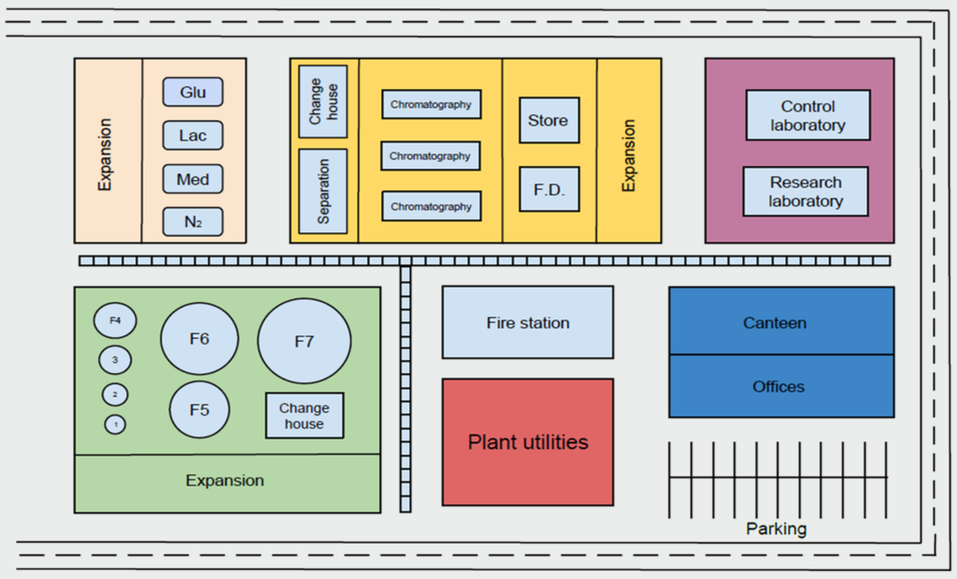
All the pictures were obtained from [1].

BLOCK DIAGRAM



The complexity of the process is shown through the block diagram. The downstream process contains several stages to safeguard the purity of the protein and that is why it is the most expensive and difficult phase.

PLANT LAYOUT



The layout is specially designed to guarantee the biosafety level 2 and to see the disposition of some elements. The plant will be located at Brazil, because the raw materials are cheaper and, in America, there is a strong hemoglobin market.

CONCLUSIONS

Hemoglobin is a very important protein in the organism, so it is interesting to produce it on an industrial scale. Biotechnology makes this process possible, which will save lives and also represents a great breakthrough in Science.

BIBLIOGRAPHY

[1] Liu L, Martínez J. L, Liu Z, Petranovic D, Nielsen J. Balanced globin protein expression and heme biosynthesis improve production of human hemoglobin in *Saccharomyces cerevisiae*. Met Eng. 2014; 21: 9–16.

Palomares L, Estrada-Mondaca S, Ramírez O. T. Production of recombinant proteins: challenges and solutions. Methods Mol Biol. 2004; 267: 15–52.