Design of a recombinant tissue plasminogen activator production plant

1

GENERAL VISION AND PRESENTATION OF THE PLANT

Authors: Carla Sánchez, Ramon Roca i **Ferran Vila**
Tutor: Prof. Carles Solà

Biotechnology Final Project, 2013
Universitat Autònoma de Barcelona

INTRODUCTION

TPA

•**Tissue plasminogen activator**(tPA) is a serine protease involved in the **breakdown** of the **blood clots.**

•**Tenecteplase** (TNK) is a **recombinant** variant of the tPA, which has higher fibrin specificity and greater resistance to inactivation.

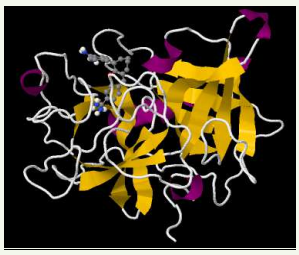


Figure 1. Crystal structure of tPA

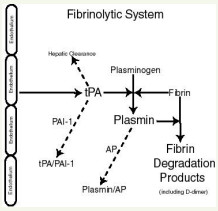


Figure 2. The blood clotting cascade where acts tPA

•**Approved** by *Food and Drug Adminsitration* (FDA) in the year 2000.

•It is used for **treating cerebrovascular diseases** caused by blood clots.

OBJECTIVE OF THE PROJECT

PRIMITIVE PROBLEM: Design a process for producing tPA in China.

SPECIFIC PROBLEM: Produce 30 kg / year of TNK, which cover about 5% of cases of cerebrovascular disease China.

MATERIALS AND METHODS

SuperPro Designer is a simulator that facilitates the planning, modeling, evaluation and optimization of processes. Once the search for information, knowing the equipment, the operations that are carried out in each one and the inputs and outputs, we can make balances and economical calculations.

Autodesk AutoCAD is a computer-aided design software for drawing in two and three dimensions. Having defined the flow will allow us design the layout.

DESCRIPTION OF THE SOLUTION

Blocks diagram | **Flow diagram** | **P&I Diagram** | **Lay-out**

PROCESS SUMMARY

The process consists of three parts clearly separated:

Upstream (Blue). Preparation of raw materials and inoculum. Duration: 10 days.

Reaction (Red). In continuous with immobilized cells. Medium flow: 500 L/h.

Downstream (Black). Separation and purification of the product of interest.

The technical characteristics of the process are specifically addressed in the second poster.

ECONOMICAL SUMMARY

Capital Investment Charged to This Project	**1039 millions $**
Payback Time	**2.58 years**
Unit Production Cost	**1.46 millions $/kg**
Unit Production Revenue	**25 millions $/kg**

The comprehensive economic analysis is the third poster.

PRESENTATION OF THE PLANT

We have an area of **50.000** m^2 in China

Different areas depending on if required sterility:

•**Offices** (Red)

•**Production area** (green)

- •All entries in this area should be controlled. Everything in and out of there must have been previously sterilized, maintaining these conditions at all times.

•**Truck's circuit** (blue)

- •We thought it appropriate to make a separate entry and exit of trucks to ease traffic and minimize maneuvering in and out of the docks.

•**Parking** for employees and visitors.

The entire facility is **fenced** and all inputs are guarded.

1. Checkpoints

1. Input from outside and dressing rooms
2. Laboratory
3. Toilets
4. Production area
5. Store of the raw materials
6. Store of the final product
7. Liquid storage tanks

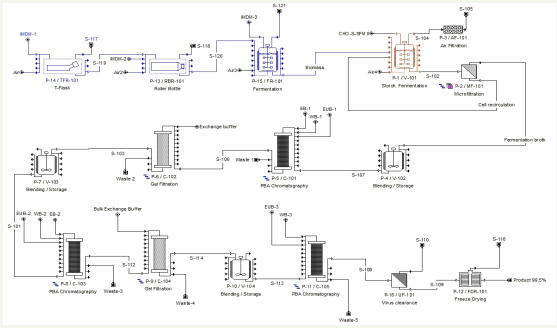
1. Toilets
2. Offices
3. Auditorium
4. Offices and meeting rooms
5. Cafeteria
6. Input from outside
7. Input from the parking

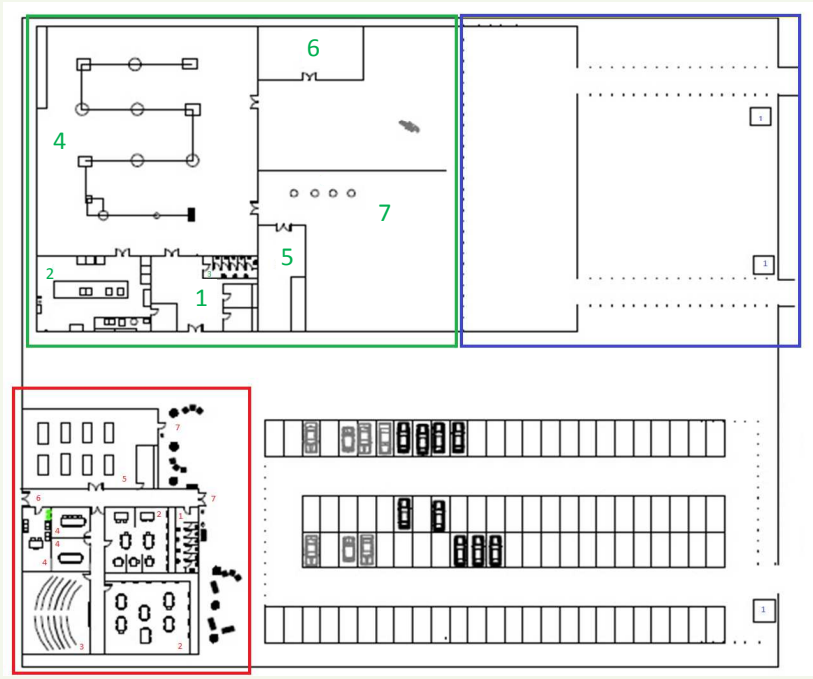
•**MAIN CHARACTERISTICS OF THE PROCESS**

•**Continuous operation**, operating for three months. **Perfusion.**

•CHO cell line DUKxB11. **Immobilized cells.**

•Production of **30 kg / year** of TNK.





SUMMARY AND CONCLUSIONS

We have built a plausible flux diagram, and a possible lay-out of a plant to produce TNK. Although it is an approach, it seems to be an economically viable project.

REFERENCES

Gennova biopharmaceuticals. (2012). WO 2012/085933 A1. World Intellectual Property Organization.
For the query of most commodity prices: **Alibaba Portal. Available on the website: www.alibaba.com/**
Prices media used: Invitrogen catalog. **Available on the web: https://products.invitrogen.com/**