Novel Strategy for Media formulation Development

Hemlata, Seongkyu Yoon,

Department of Biomedical Engineering and Biotechnology

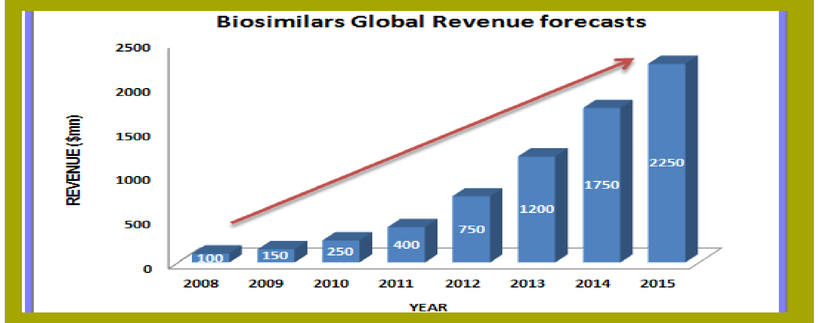
University of Massachusetts, Lowell ,MA-01854

Abstract

Biosimiliar market is growing very fast. Media formulation is a critical step in biosimiliar development as the process is labor intensive and time consuming. The proposed strategy can reduce the time for media development significantly. The approach to develop the strategy includes media formulation for a particular cell line by using spent media analysis followed by regression modeling. The up or down regulation of genes associated with different metabolic processes as a function of various media components can be explained by performing gene expression analysis of cells grown in different media compositions. This strategy is supposed to decrease the time for media development significantly.

Introduction

1. Biologics are moving into top sale drug. Product yield is the key goal to achieve. Product yield drives the manufacturing capacity, drug cost and availability. To improve the process, media is one of the critical parameters to focus on.



Source: Stelllarix consultancy services

2. Each cell line has its own requirements of nutrients and cell culture media typically consists of many components. So media development for a particular cell line is very time consuming.

3.A strategy, which can reduce the time to some extent will contribute significantly to the process cost and availability.

Approach

1. Media formulation

- Spent media analysis
- Design of Experiment

Run/Media Component	A	B	C	D	E	Cell Growth	Titer	Glycosylation
1	-1	-1	-1	1	1			
2	-1	-1	1	1	-1			
3	-1	1	-1	-1	-1			
4	-1	1	1	-1	1			
5	1	-1	-1	-1	1			
6	1	-1	1	-1	-1			
7	1	1	-1	1	-1			
8	1	1	1	1	1			

2. Regression Modeling

$P_1 = a_1X_1+a_2X_2+a_3X_3.....$

$P_2 = b_1X_1+b_2X_2+b_3X_3.....$

$P_3 = c_1X_1+c_2X_2+c_3X_3.....$

➢**Objective**

Max ΣC_iP_i s.t. $P_1<P_3 = f(x)< P_2$

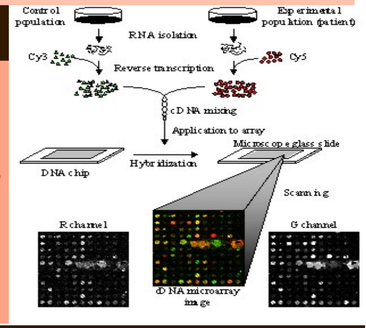
Where P_1 is VCD,

P_2 is product titer and

P_3 denotes the product quality attributes.

3. Microarray

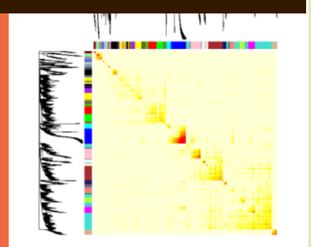
Microarray of all the samples from DOE can give the information about gene expression profile (Upregulation or downregulation of genes).



4. Linkage of gene activation to media components (Weighted Gene Correlation Network Analysis)

- Gene regulation can be linked to
- Different media components

- Genes responsible for different
- Properties can be identified.
-



Expected Outcome

- Regression model between required outcome and different media components
- Identification of genes responsible for favorable outcomes i.e. cell growth, product titer and product qulaity attributes.
- Identification of specific media components responsible for up or down regulation of specific genes.
- With the help of this information, by mapping the microarray information of a cell culture sample of particular cell line, initial composition can be decided in a very short span of time, which can reduce the time of media development to a significant time.

References

- http://labs.genetics.ucla.edu/horvath/CoexpressionNetwork/OverviewWGCNA.pdf
- http://www.nicb.dcu.ie research_cho_bioinformatics.html
- http://labs.genetics.ucla.edu/horvath/CoexpressionNetwork/Rpackages/WGCNA/#WGCNAIntro
- http://www.stellarix.com/blog/review-on-the-current-and-future-trends-of-biosimilar-market-in-usa-and-india/
- http://www.colorimageprocessing.com/research_cDNA1.html
- http://biogeeks.wordpress.com/2011/06/09/june-tech-meet/

Contact

Hemlata
Hemlata_hemlata@student.uml.edu

Seongkyu Yoon, Ph.D.
Seongkyu_yoon@uml.edu
Ph. No. 978-934-4741