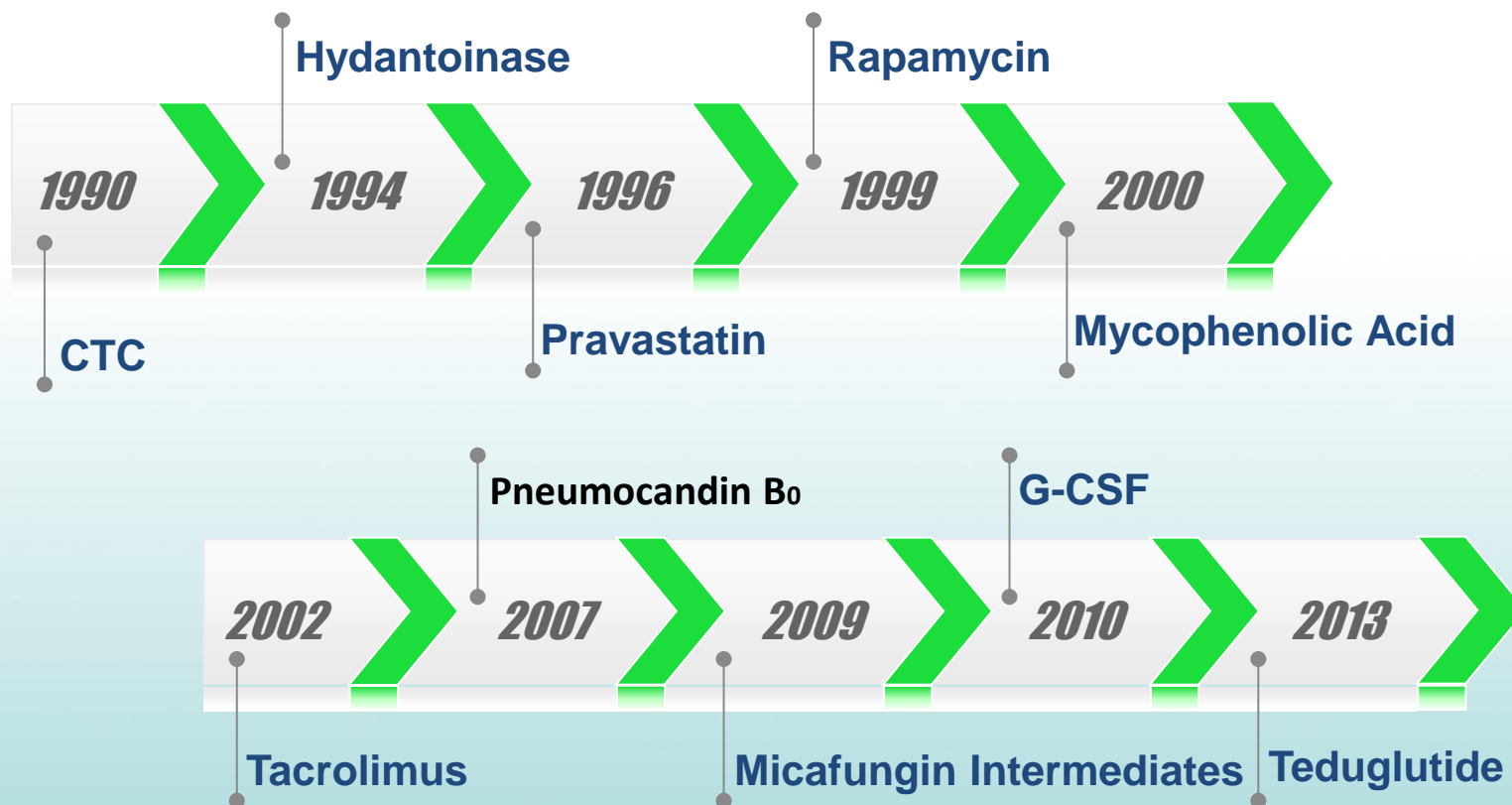


How to develop fermentation API at CCSB

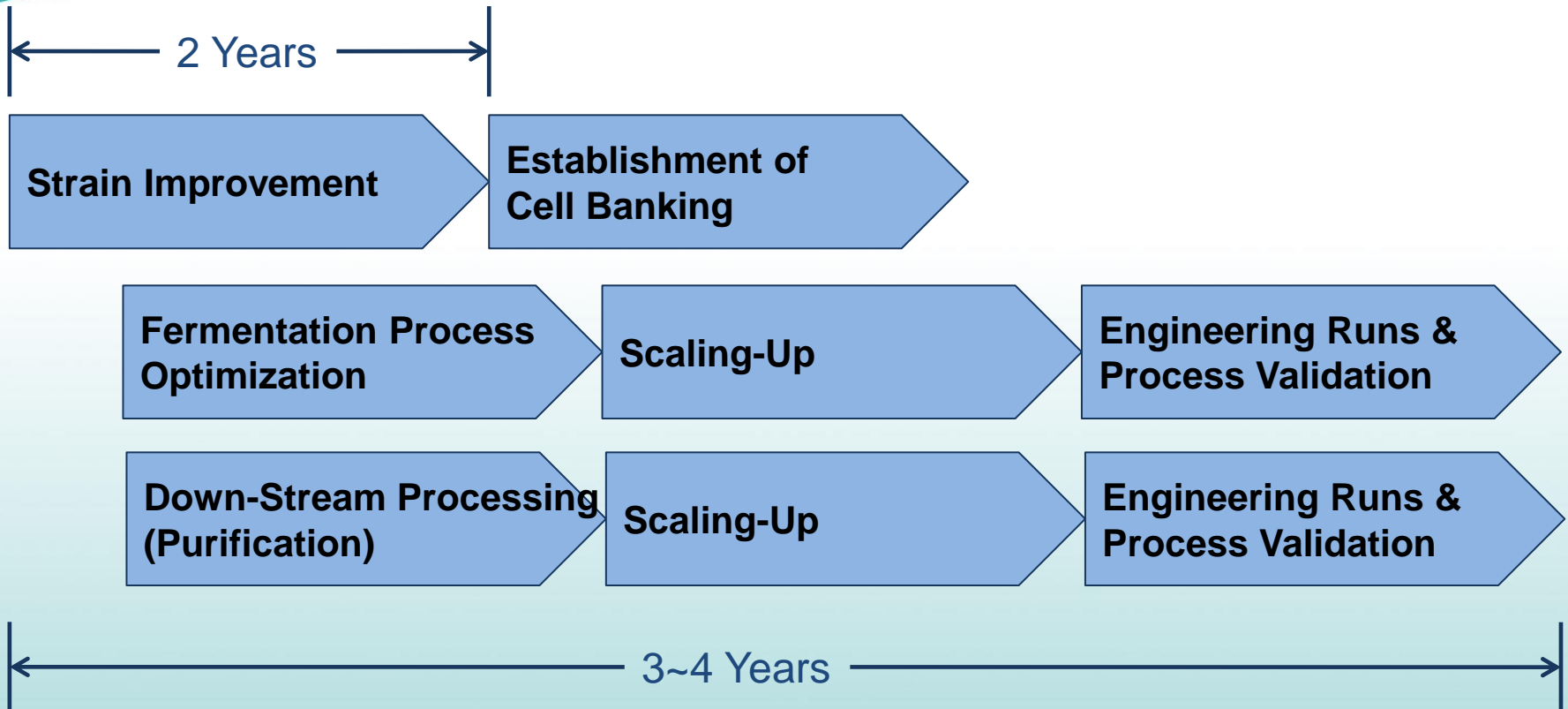
Update:08/21/2020



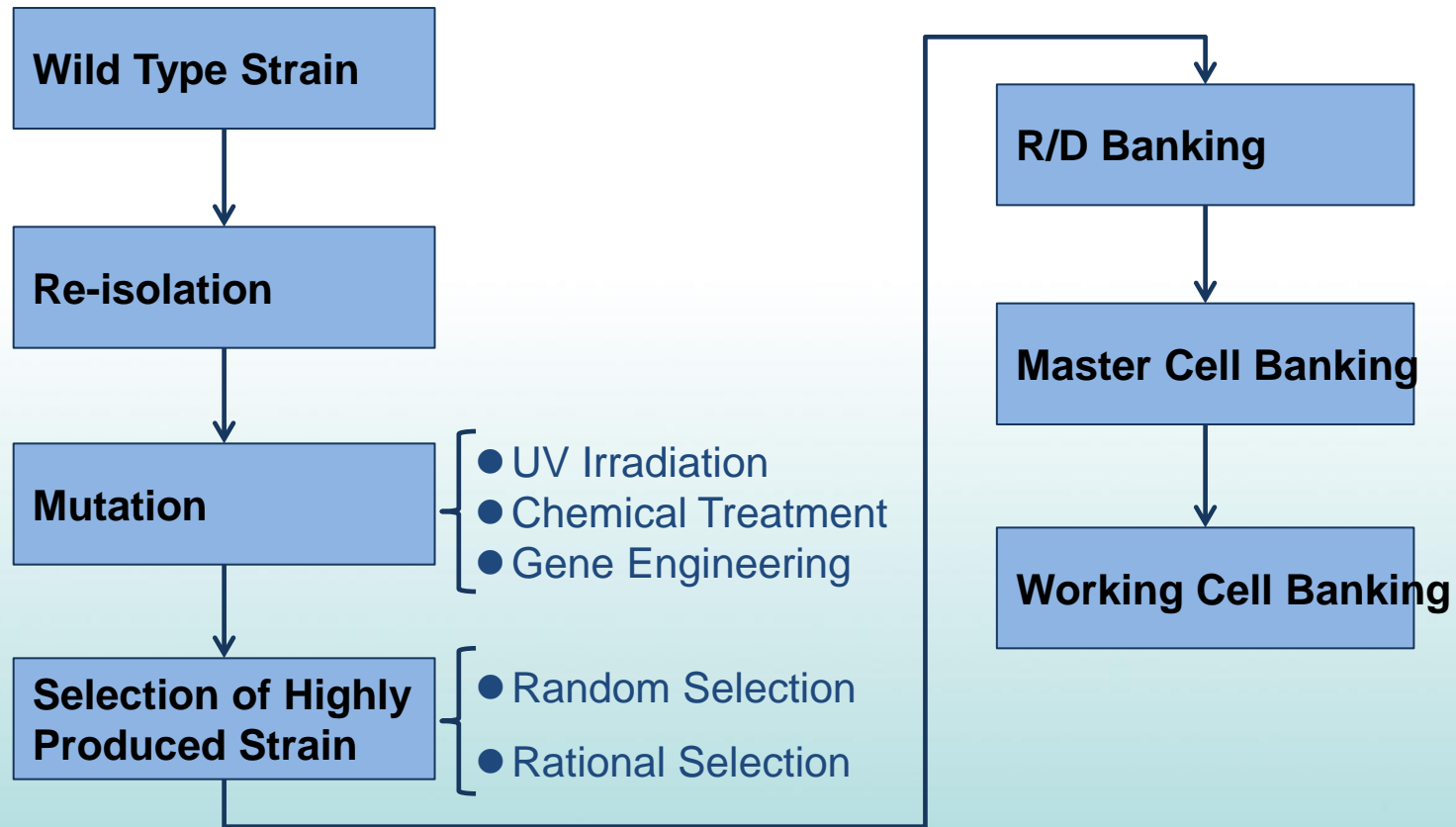
More Than 20 Years Experience in Developing Fermentation Products



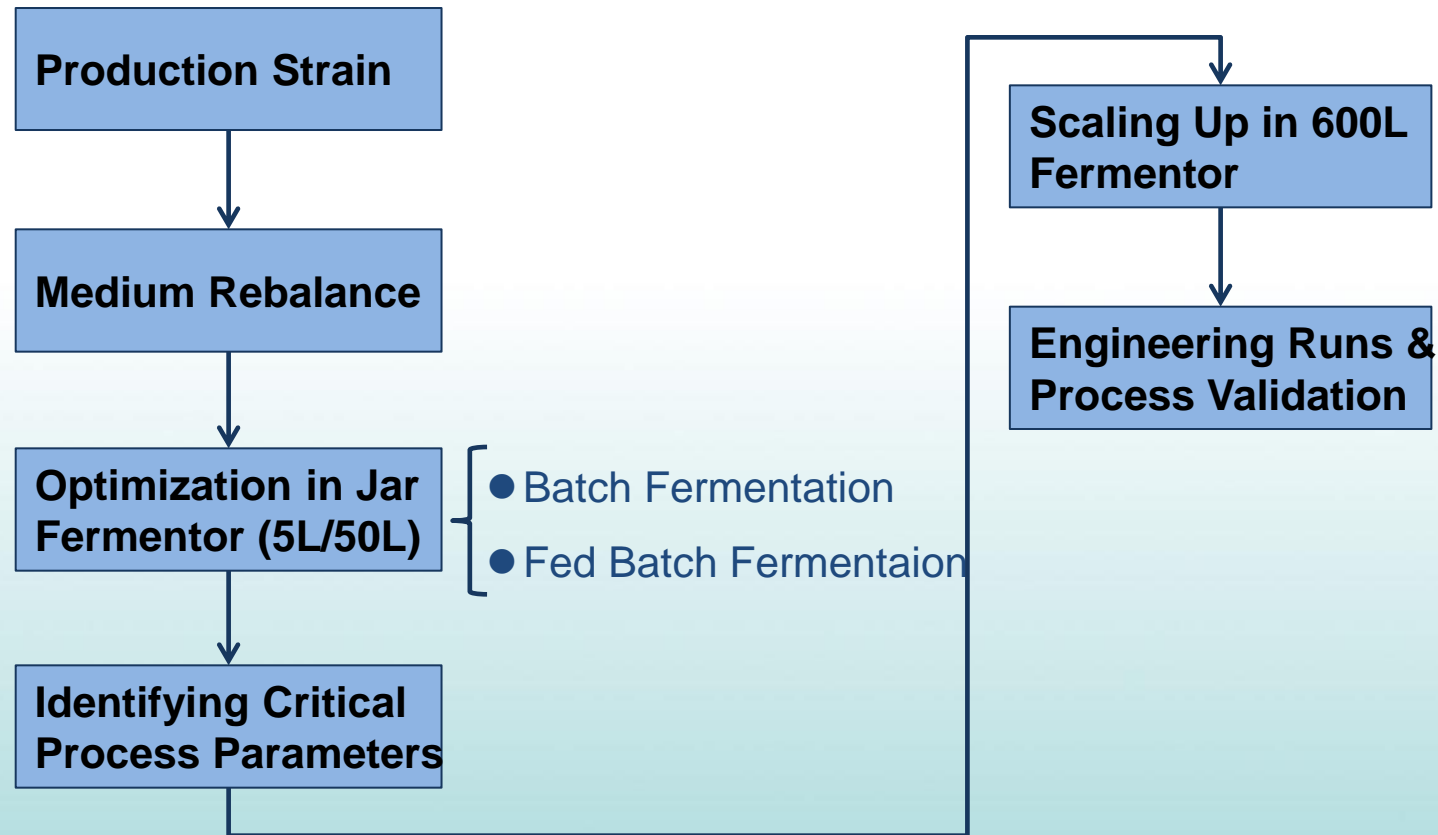
Fermentation API Development



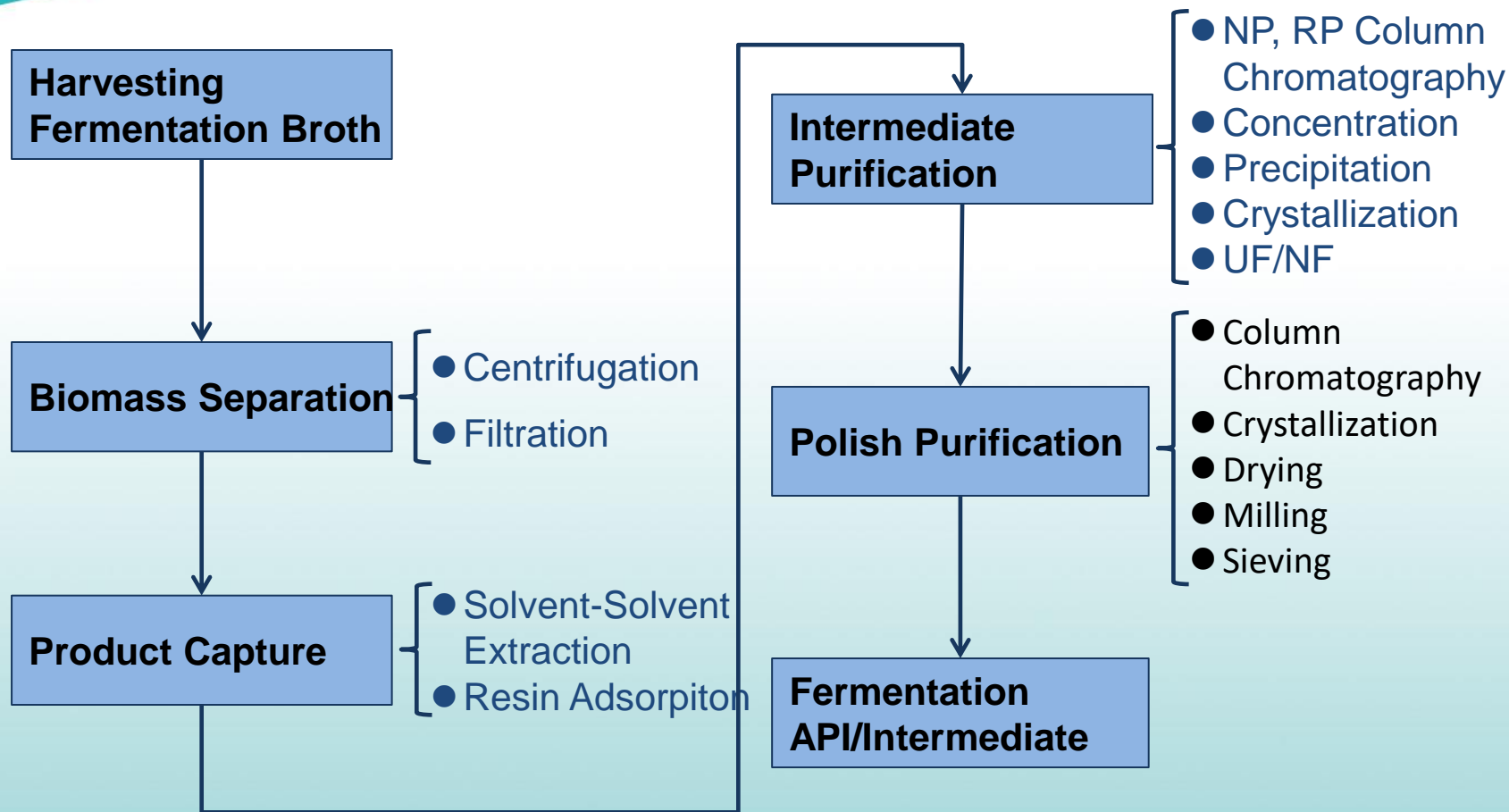
Strain Improvement Program



Fermentation Process Optimization



Down-Stream Processing



Systematic Approach to Recombinant Peptide



Cell line Development

- Expression system selection
- Vector preparation
- Stable clone generation
- Scale-up
- Development bank
- Clone characterization
- Stability
- Bioreactor evaluation

Cell Culture/ Fermentation Process Development

- Cell line
- Media development
- Cell expansion
- Parameter optimization
- High cell density culture
- Robustness study
- Scale-up

Systematic Approach to Recombinant Peptide



Purification Process Development

- Ion Exchanger Column
- Affinity Column
- HIC Column
- SEC Column
- Refolding
- Preparative HPLC
- Lyophilisation
- Scale-up

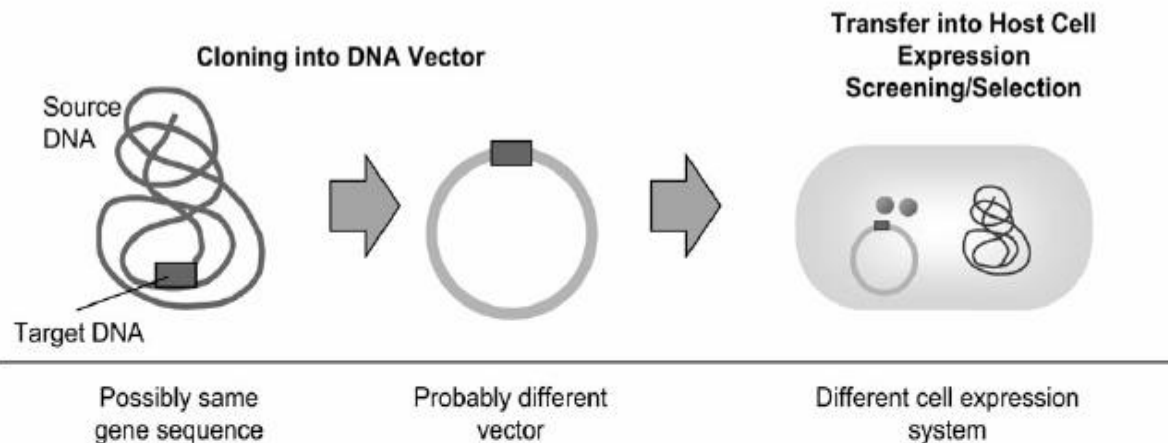
Analytical Method Development

- Characterization
- Chemical Assay
- Bioassay
- Bioburdens
- Impurity Profiling
- Degradation Profile
- Method Validation

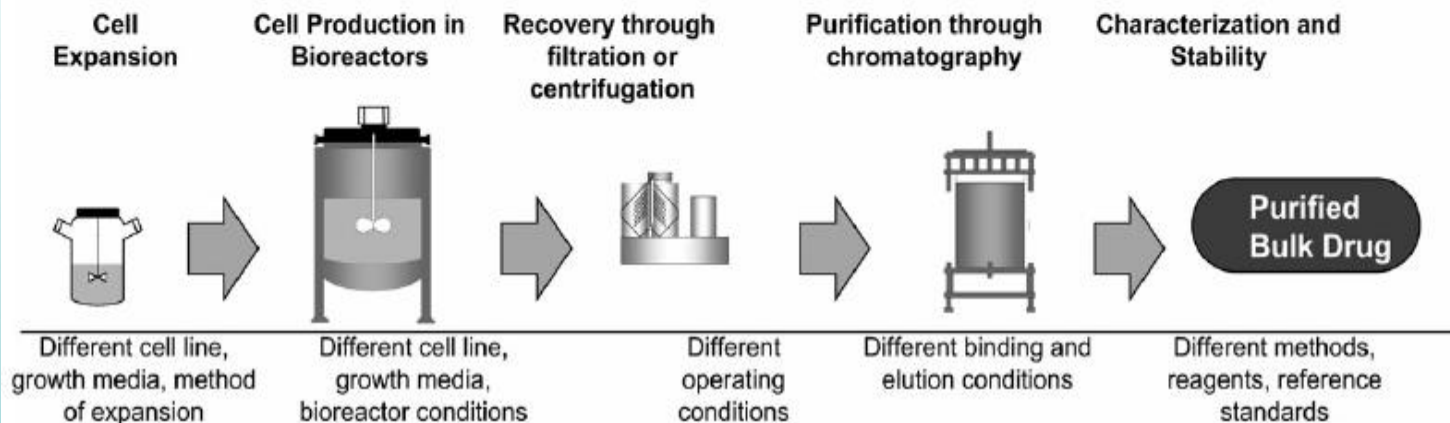
Recombinant Protein Production



Cloning and Protein Expression



Protein Production, Purification and Validation



Recombinant Peptide Production



Pros

- Relatively inexpensive and simple to perform
- Versatile hosts and expression vectors
- Extensive knowledge regarding DNA manipulation
- Easy manipulation of expression host system
- Efficient and cost-effective high production yields
- Mature scale up and purification system

Cons

- Expression of all natural amino acid peptides
- Purification of low molecular weight peptides
- When Met is not the first amino acid in mature peptides
- Aggregation
- Host cell proteins and DNA

Strategy of Recombinant Cell Line Construction



Fusion protein technology

- Enhance expression of target protein
- Improve protein solubility
- Easy to be purified via tag
- Highly solubility in native buffers

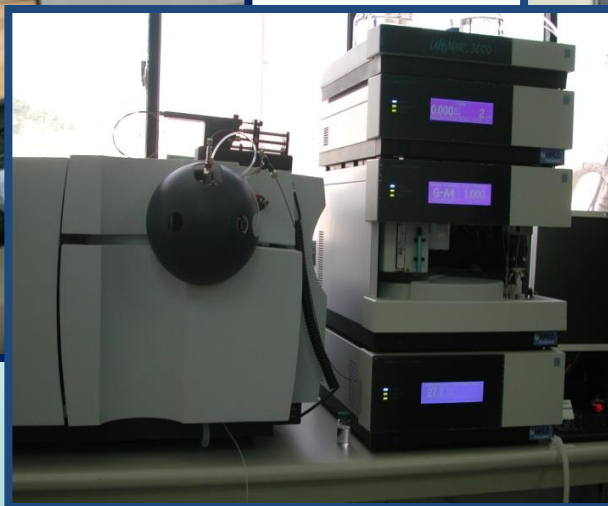
Innovation technology platform

- Construct novel fusion protein expression vector
- Enhance peptide expression level, improve solubility
- Fusion protein can be efficiently cleaved by inexpensive enzymes

Instrumentation (cont.)



GC/MS



LC Mass

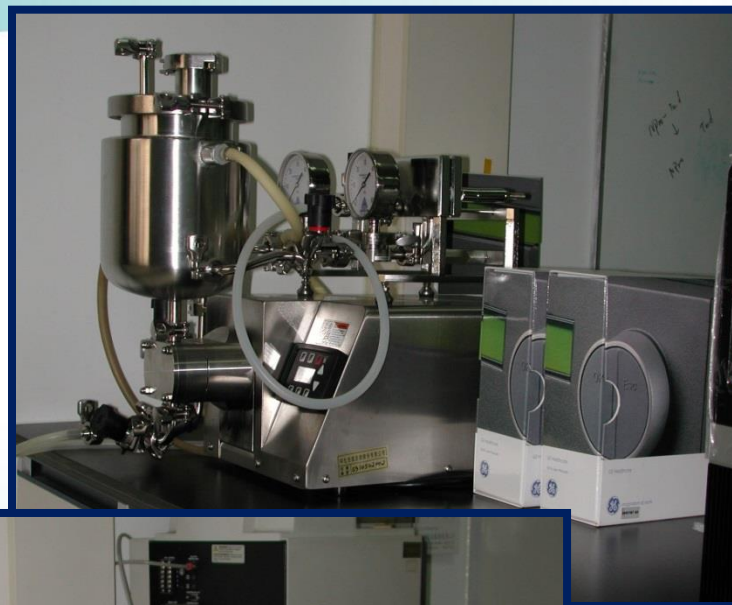


UPLC

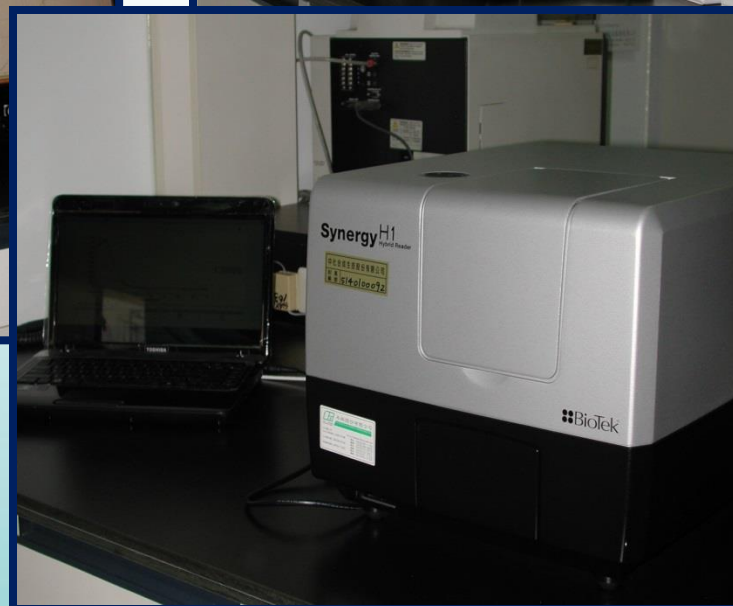
Instrumentation (cont.)



GE AKTA Purifier UPC



**BioTek Synergy H1
Hybrid Reader**



**KvickLab Cross
Flow System**

Instrumentation (cont.)



Mbraun Glove
box

Type: UNILAB-B

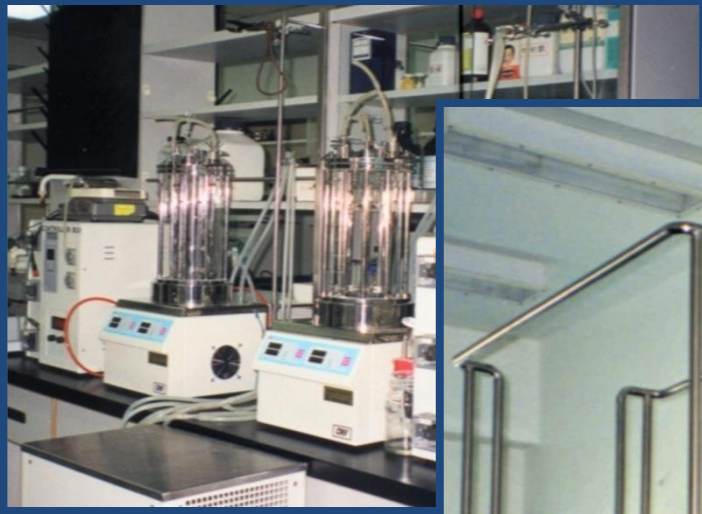


Bio Rad ChemiDoc XRS+ Imaging
System

Biotech Pilot Plant



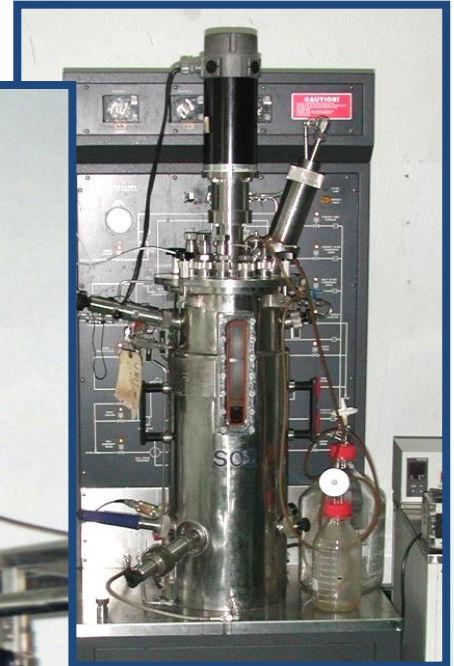
CCSB



5 L Fermentor



600 L Fermentor



22 L Fermentor



Thank you for your attention!