



# **Biopharmaceutical Industry Perspective on Knowledge Transfer**

Jonathan Klein-Evans  
Vice President, Intellectual Property  
MedImmune  
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# Where complex knowledge lies

- Sources of molecules (Libraries)
  - ◆ The molecules themselves
  - ◆ Methods of generating (synthetic, natural, both)
  - ◆ Methods of screening
  
- Enhancements
  - ◆ Methods of predicting
  - ◆ The modifications themselves
    - > Activity
    - > Formulation
  
- Manufacturing
  - ◆ Scale up
  - ◆ Efficiency
  - ◆ Yield

# The knowledge gets out

- Innovative drug development costs requires enormous up-front at-risk investment
- Patents provide opportunity to gain a reasonable return on investment in innovation
  - ◆ To *apply* for a patent essentially means to publish
  - ◆ When patents are hard to enforce, trade secrets may be preferable
    - > Manufacturing processes
  - ◆ Challenge to maintain secrecy in today's mobile economy and digital age
- Technology is publicized
  - ◆ Through advantages of patenting
  - ◆ Through scientific literature to attract employees and collaborators

# The two-way flow of information

- In-licensing/collaboration: Bringing in technology and partnering development
  - ◆ Business Development group crucial to R&D growth
    - > Industry and scientific conferences, venture partnering, etc.
  - ◆ Cost/benefit sharing have become more flexible
  - ◆ All stages – from early research to late stage development
  
- Out-licensing: The broader the technology's application, the less incentive to lock it up
  - ◆ Only so many drugs can be supported through clinical trials by any one company
  - ◆ IP rights provide return without additional investment through out-licensing
  
- Inhibition of flow of ideas to market is not access to technology but cost and risk in development
  - > Patents help mitigate this risk

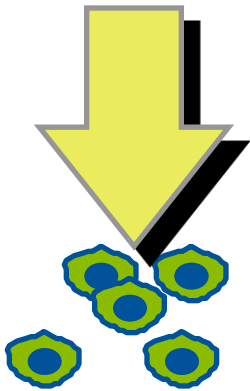


# Example 1: Phage Display

## Discovery of fully human antibodies

# Construction of $10^{11}$ scFv library

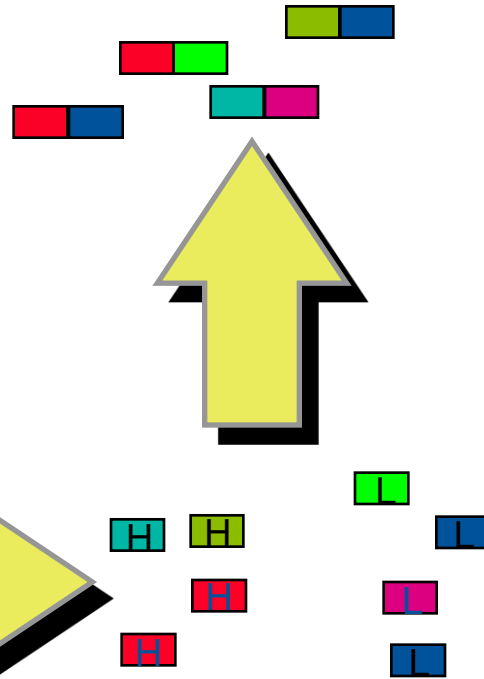
43 'non-immunised'  
donors, 7-70 yrs



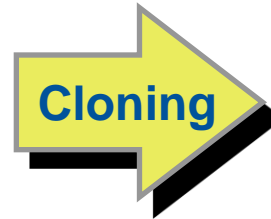
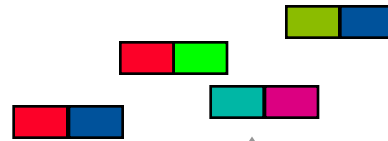
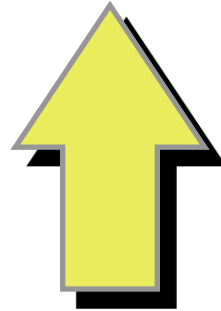
Isolated B cells



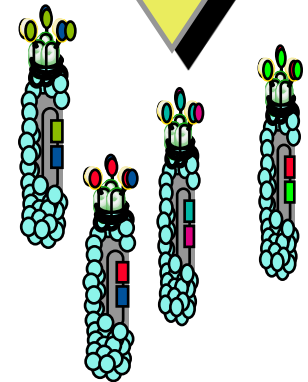
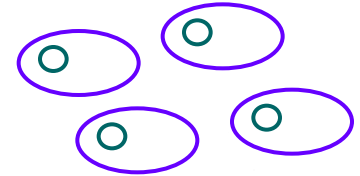
PCR amplified  
 $V_H$  and  $V_L$  genes



$V_H$  and  $V_L$  genes  
assembled as scFv

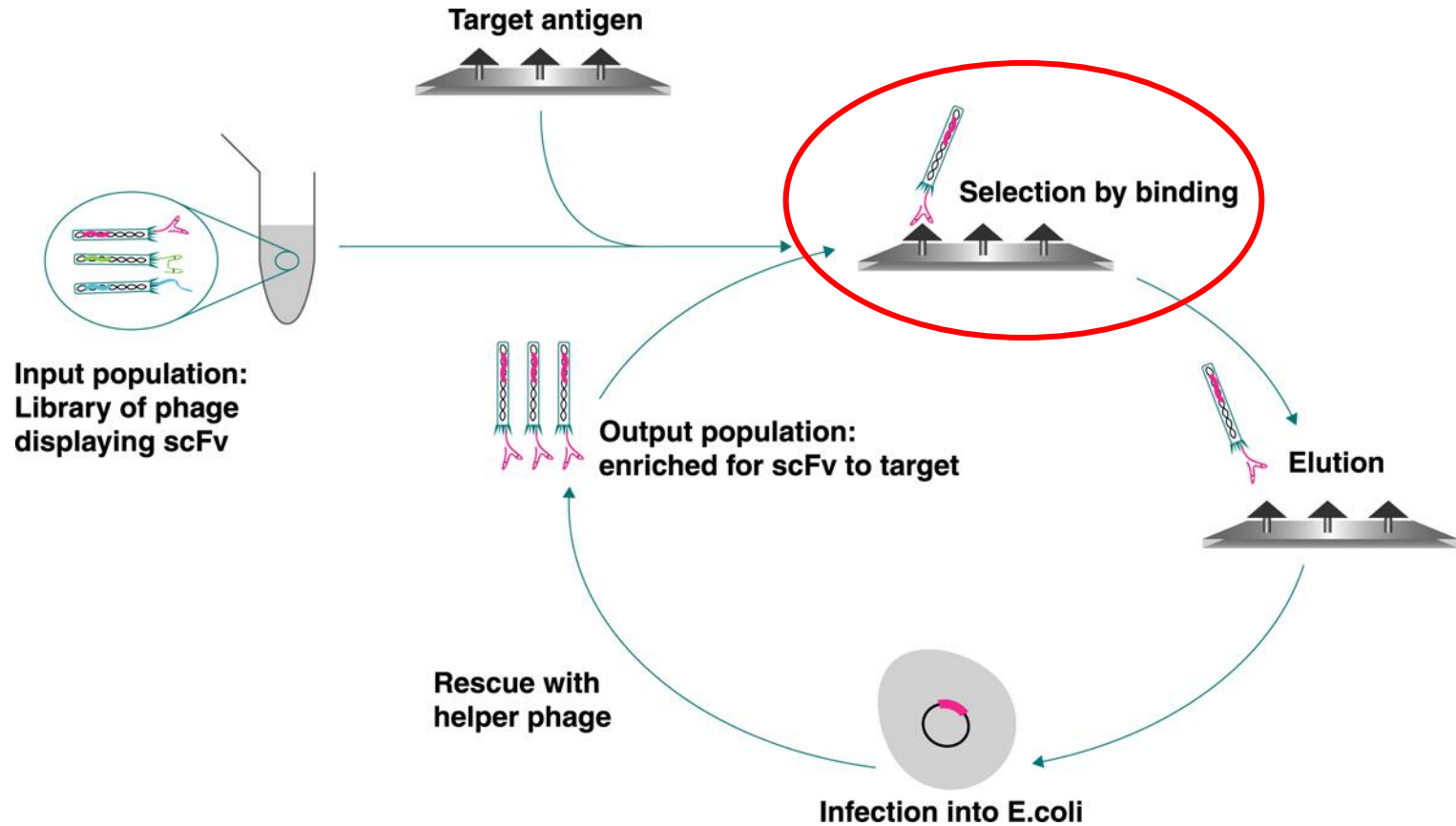


Transformed *E. coli*



Phagemids displaying  
scFv

# Phage display overview



# Phage Display Patent Complex

- MedImmune (CAT)
  - ◆ 3 distinct patent estates – libraries, display, fully human Ab's
- Dyax
  - ◆ 1 basic patent estate
- Others with pieces of IP/technology
- Others competitors commercializing discovery process
  - ◆ e.g, Morphosys
- Cross licenses arranged
- Result: dozens of licenses, technology widely disseminated
  - ◆ Basic research and to develop drugs like blockbuster Humira®

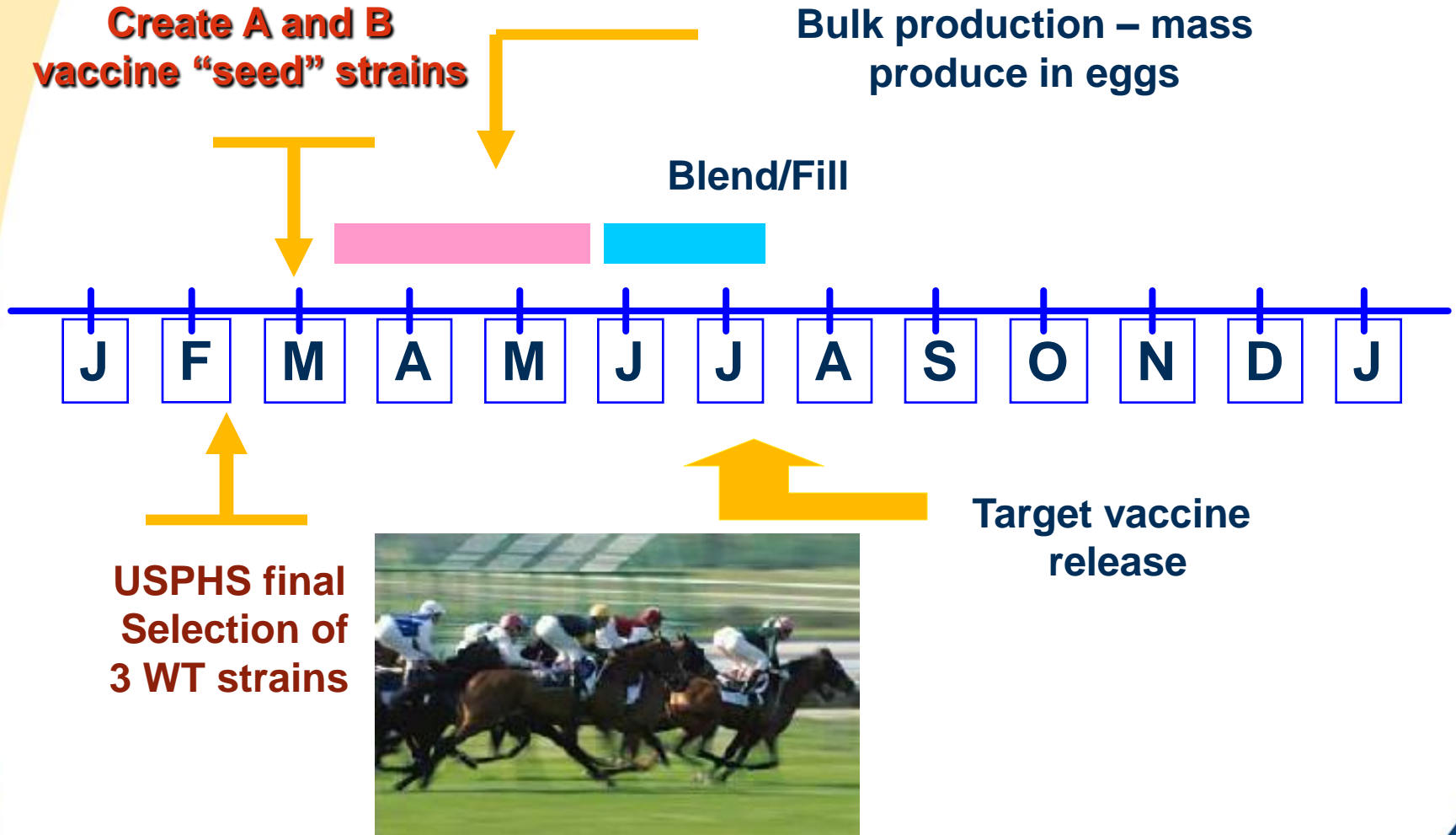




# Example 2: Reverse Genetics

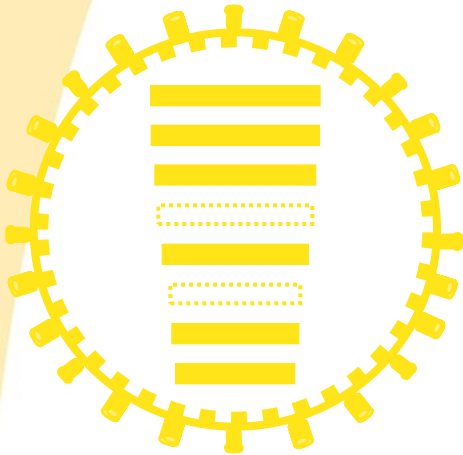
## Genetically engineered influenza

# Seasonal Flu Manufacturing Timeline



# Creating Seed Virus by Classical Reassortment

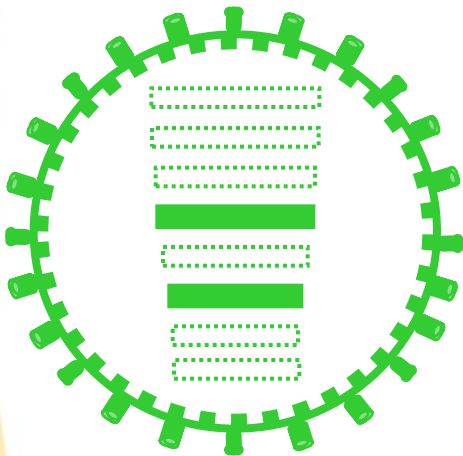
Donor virus



Co-infect



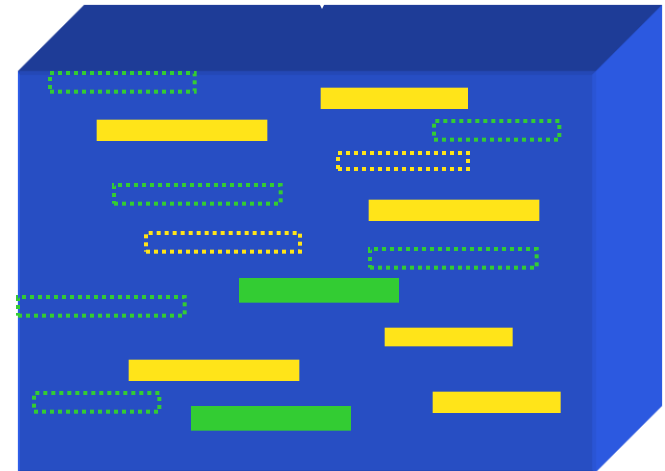
Cell



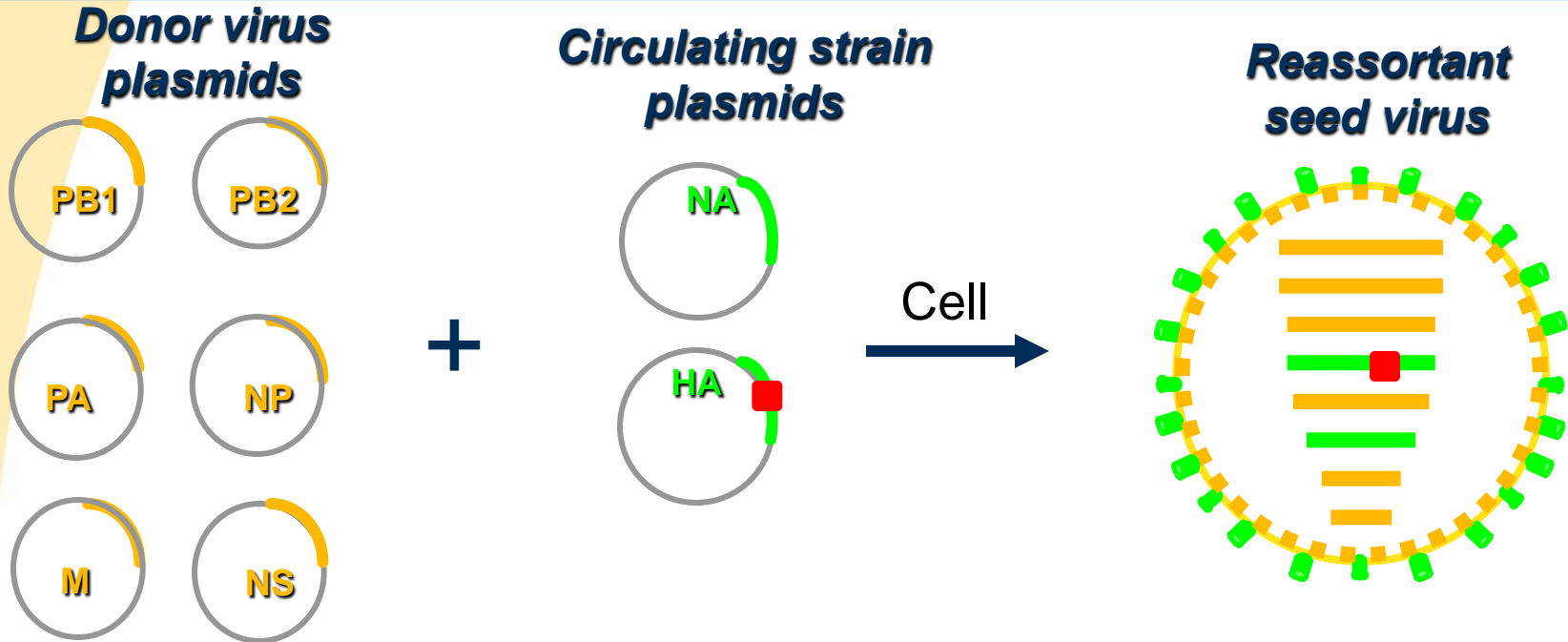
Circulating wild-type virus



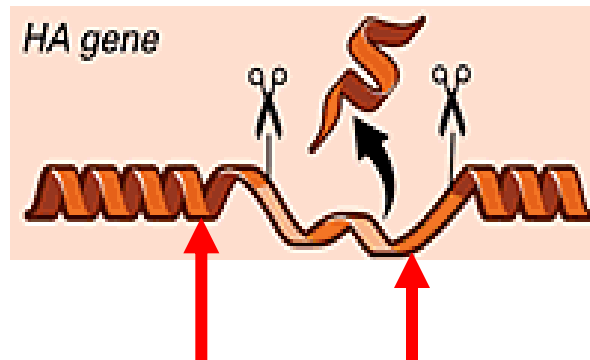
1 of 256 Reassortant Viruses is proper 6 + 2



# Creating the Seed Virus by Reverse Genetics



Optional alteration



**Removal of polybasic cleavage site and amino acid substitution**

- ✓ Shorten seasonal timeline
- ✓ Remove dangerous avian components

## ■ Medl Fundamental Reverse Genetics Portfolio

- ◆ Developed by Palese et al. at Mt. Sinai in late '80s to early '90s

## ■ Wisconsin Plasmid Rescue Portfolio

- ◆ Developed by Kawaoka et al. at U. Wisconsin in late '90s

## ■ Mt. Sinai Plasmid Rescue Portfolio

- ◆ Developed by Palese et al. at Mt. Sinai in late '90s

## ■ St. Jude Dual Promoter Plasmid Rescue Portfolio

- ◆ Developed by Hoffmann at St. Jude around 2000

## ■ Public Component:

- ◆ WHO global influenza surveillance program
  - > Collaborating centers – CDC
  - > Provide strains
  - > Cooperate with influenza vaccine manufacturers in seed generation

## ■ Private Component:

- ◆ Reverse genetics
  - > Several licenses have been granted, including to the three major influenza vaccine manufacturers

- Drug development is an expensive and risky business
- Patent rights help encourage development
- Patent rights foster knowledge dissemination and risk spreading
  - ◆ Publication
  - ◆ Licensing
- Collaboration is dynamic and growing more so
- Market forces have driven resolution of even the most complex patent situations