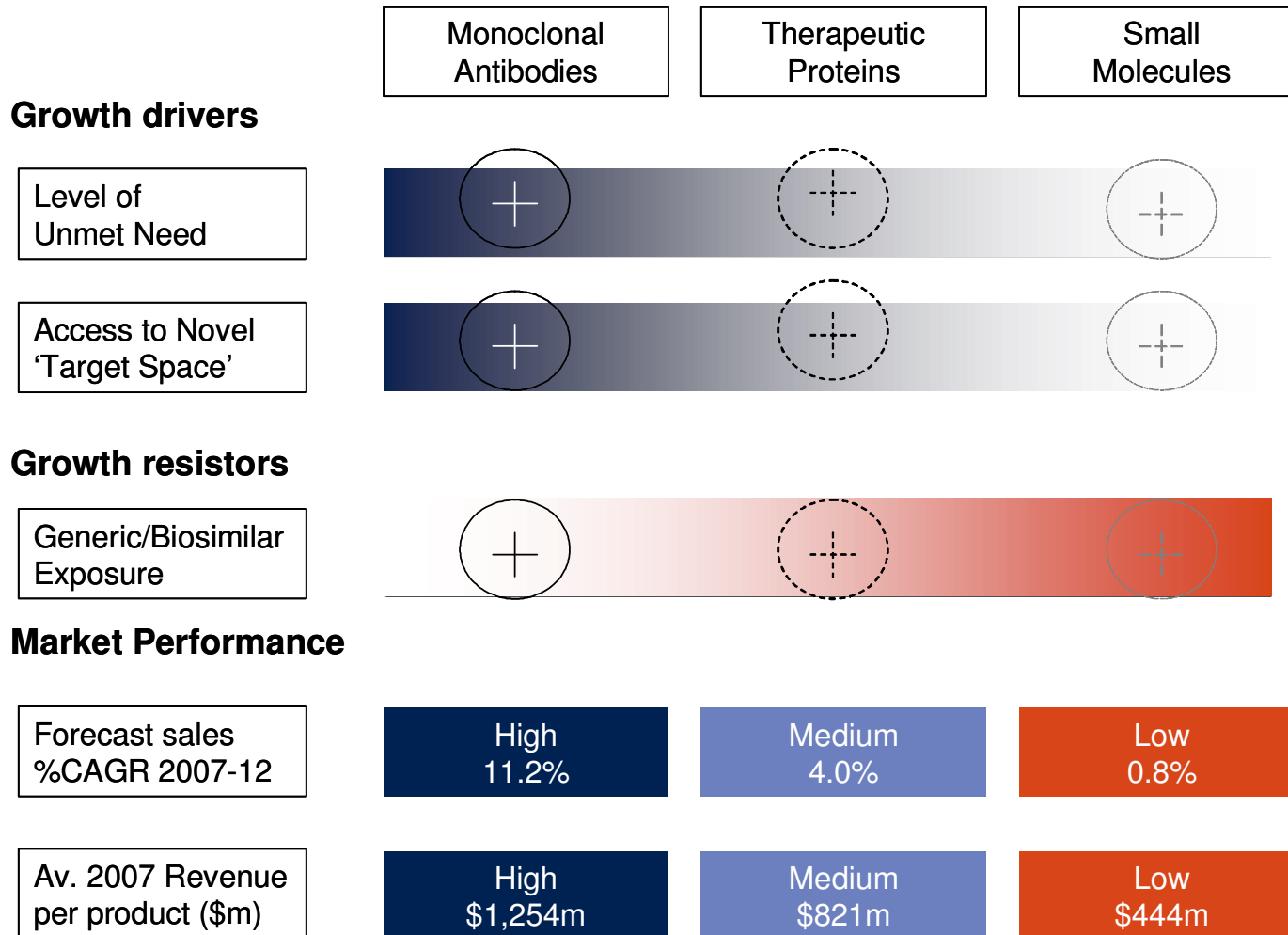
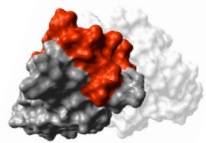


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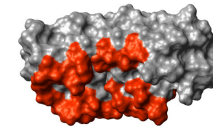
Future looks good for biologics



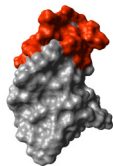
And will comprise more than just Mabs



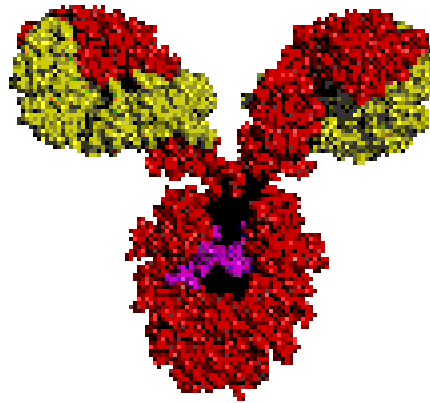
scFv



DARPin



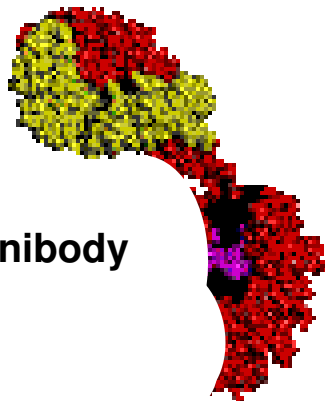
VH



IgG



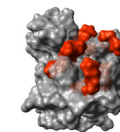
Affibody



Unibody

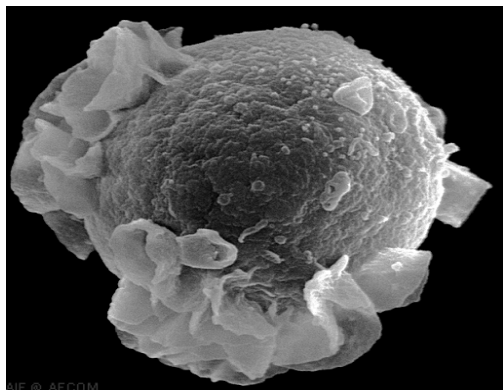


Fab

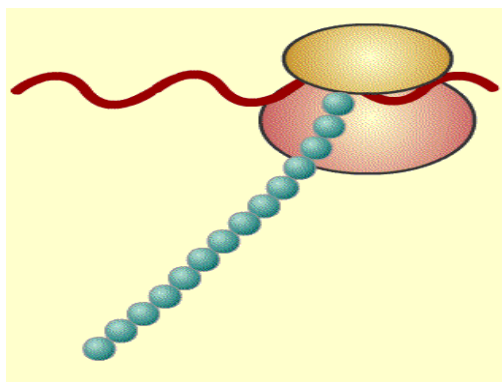


Anticalin

Created a number of ways



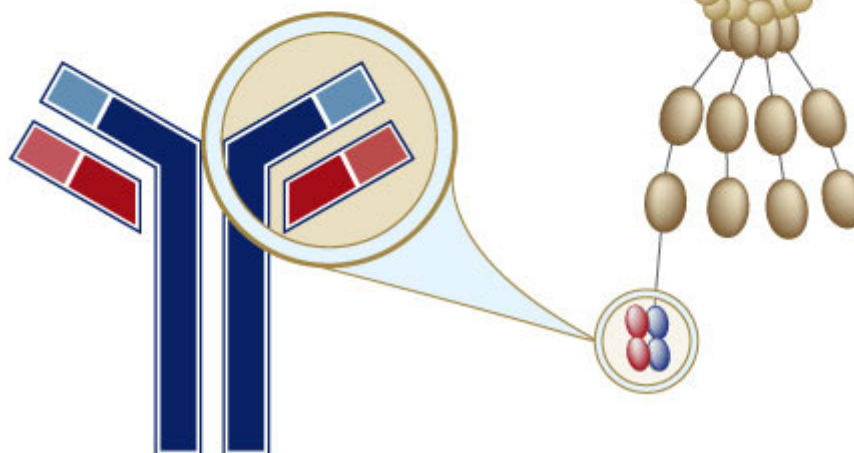
In vitro B cell immortalisation



Ribosome display

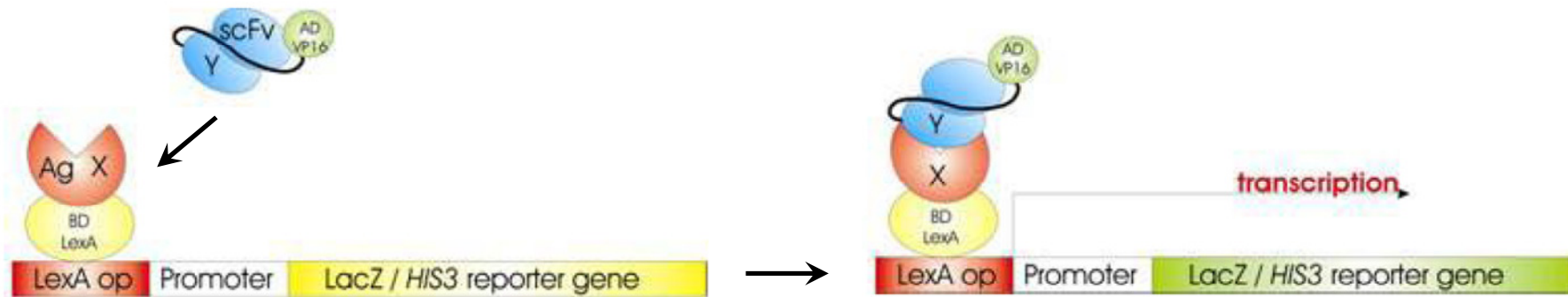


Natural or Transgenic mice



Phage
Display

Intracellular Antibody Capture Technology



- Selection of specific antibodies directly from gene sequence
- Uses yeast two hybrid system for selection
- Only scFv that bind in vivo activate the reporter genes
- Allows for screening for functionality
- Selection in reducing environment: very stable antibody molecules

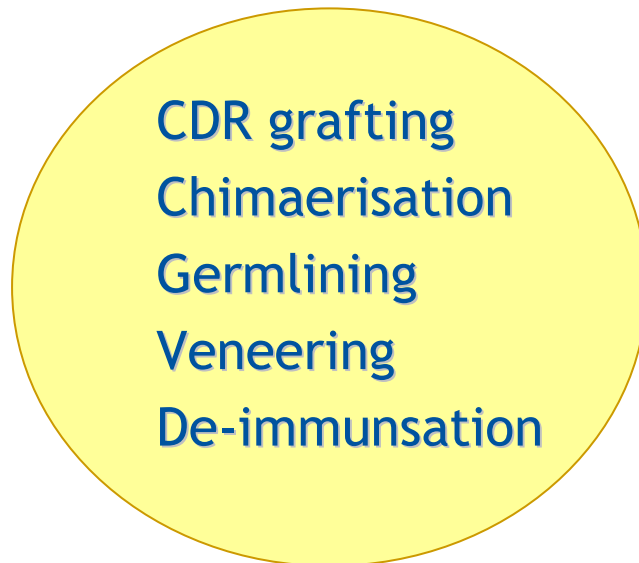
Binding Sites

- No longer just Mabs
- No longer technology limited
- Multiple routes to functionally equivalent molecules
- Impact of self-tolerance
- Technologies can be applied serially
- Screen is 'unseen' critical component
- IP expiry on early tech will be a significant driver

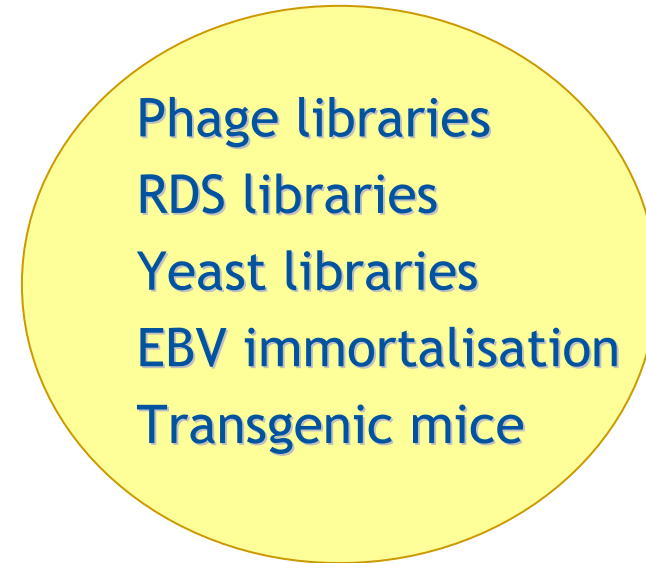
Immunogenicity

Routes to immunological 'silence'

Non human

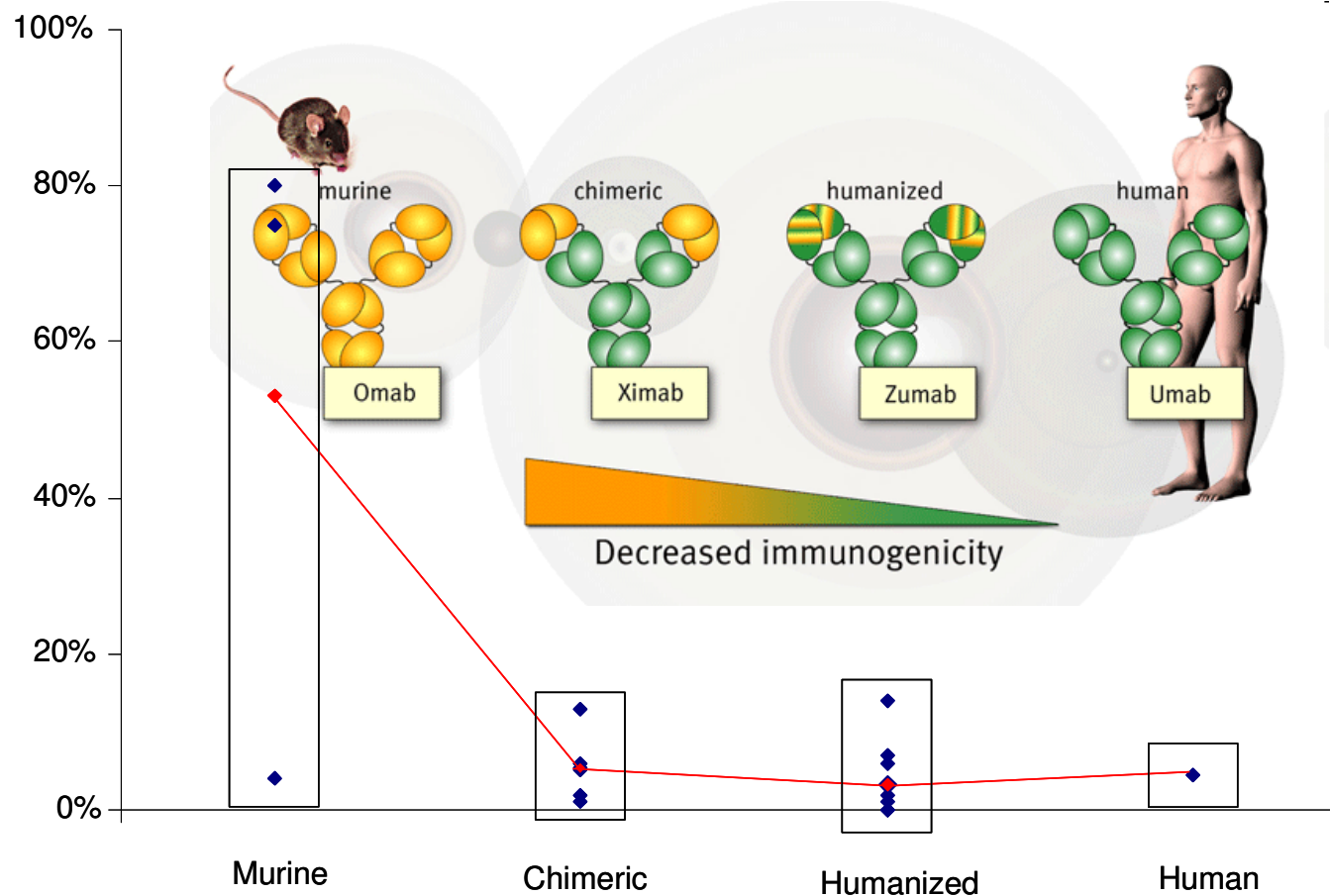


Human

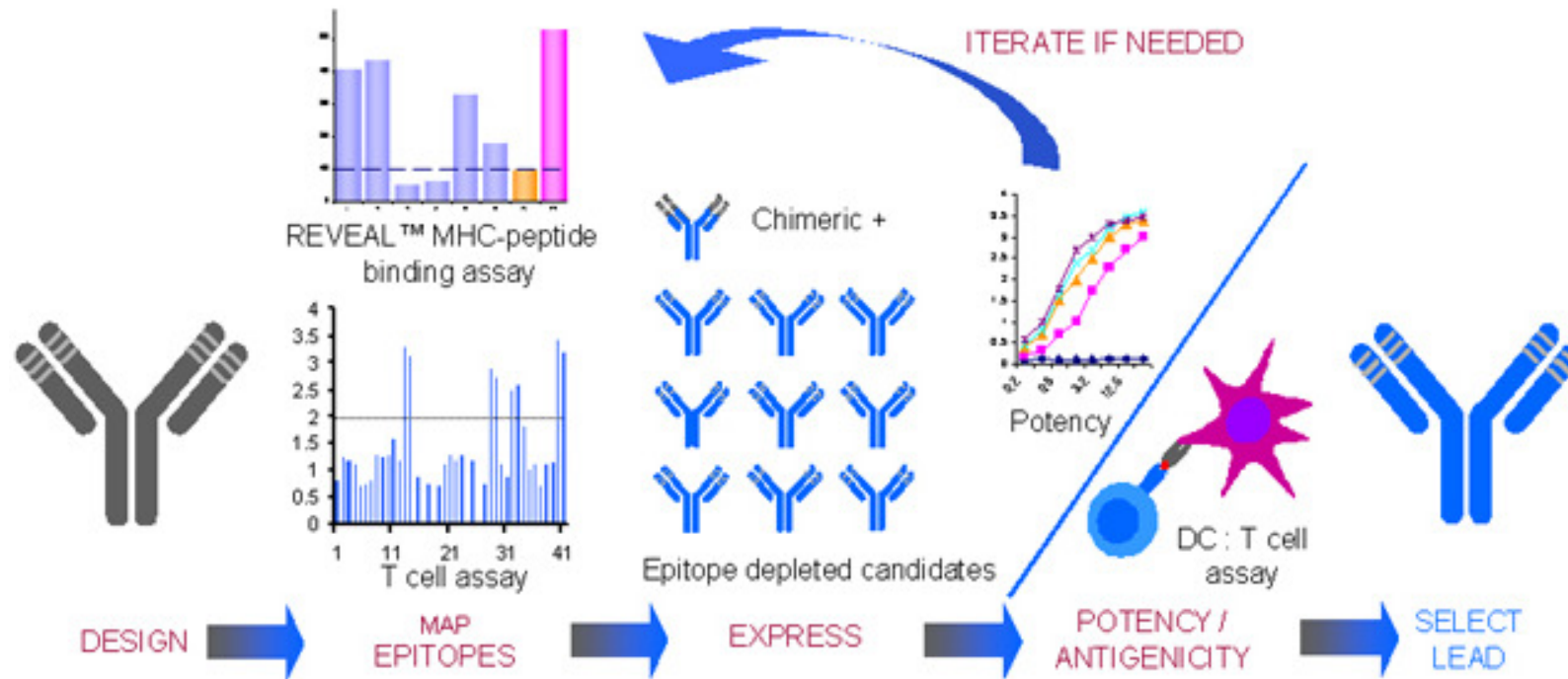


- Aim is to achieve immunological 'silence'
- Several routes possible

Immunogenicity

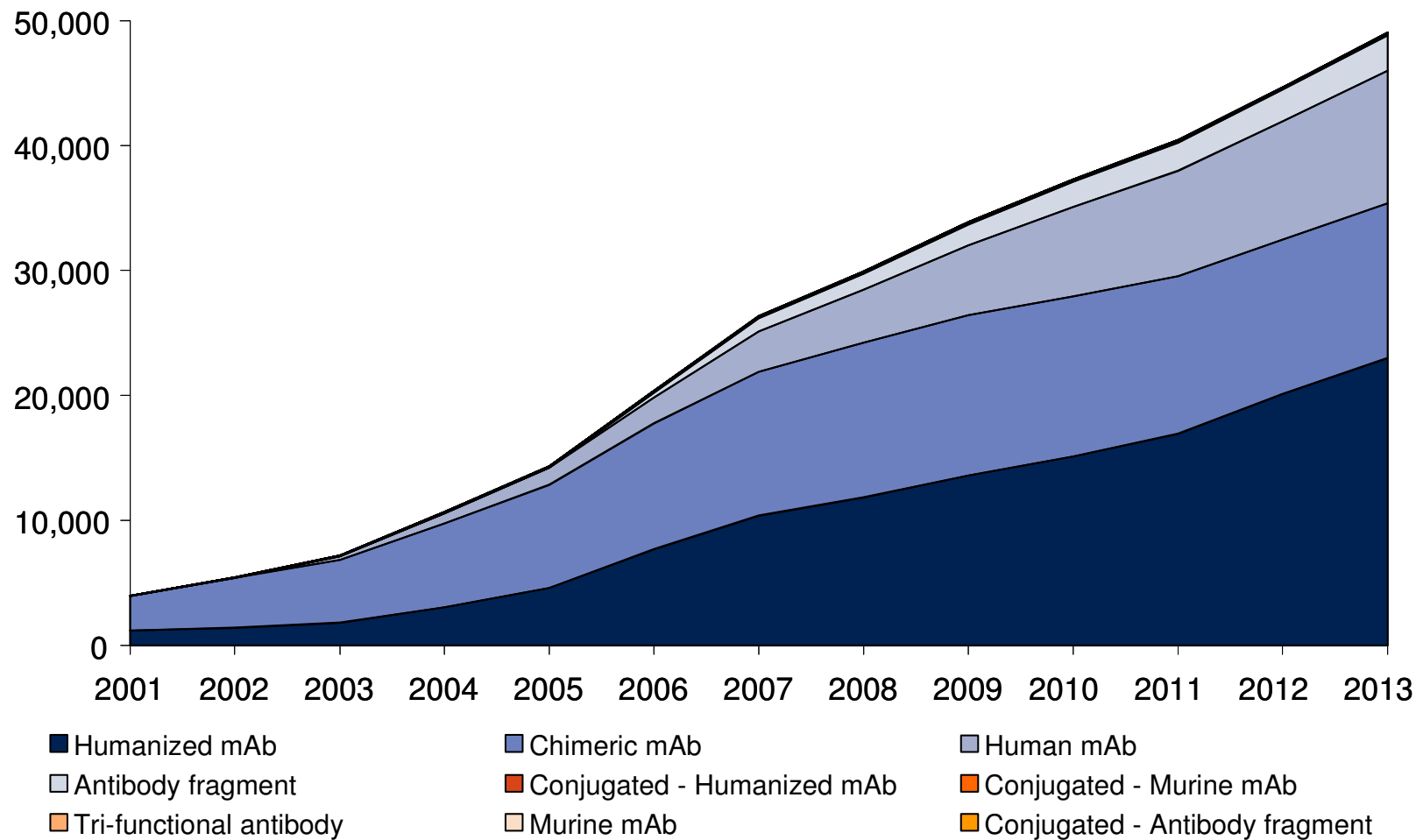


Direct Removal of T Cell Epitopes



- Select peptides that have compromised immune presentation
- Especially useful applied to proteins other than Mabs

Market continues to be dominated by Mabs



The real story is targets

Targets

Main causes of attrition

NCE

1990 40% PK & Bioavail.

2000 10% PK & Bioavail
30% Efficacy
30% Safety

Biologicals

2000 >80% efficacy

- **Toxicity/safety has a profound impact for NCE**
- **Challenge for NCE is to improve safety (selectivity)**
- **Challenge for biologicals, including Mabs, is efficacy (mostly)**

Sources of Attrition/Failure

- Target risk
 - Target role in disease pathology
- Mechanism risk
 - MOA impact on disease pathology
- Clinical indication
 - TNF Mabs were originally developed for sepsis...
- Technical
 - Safety, immunogenicity, potency
- Organisational risk
 - Infrastructure, management
- Market risk
 - Competition, clinical practice, reimbursement

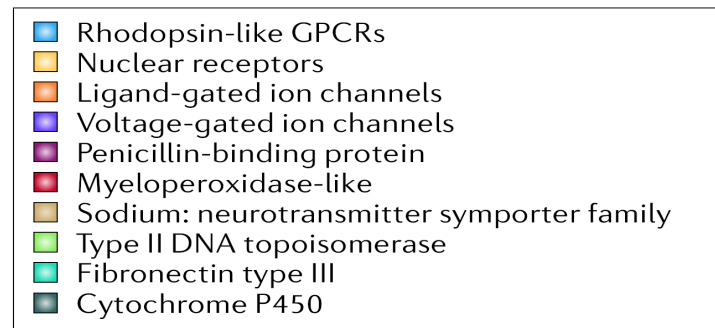
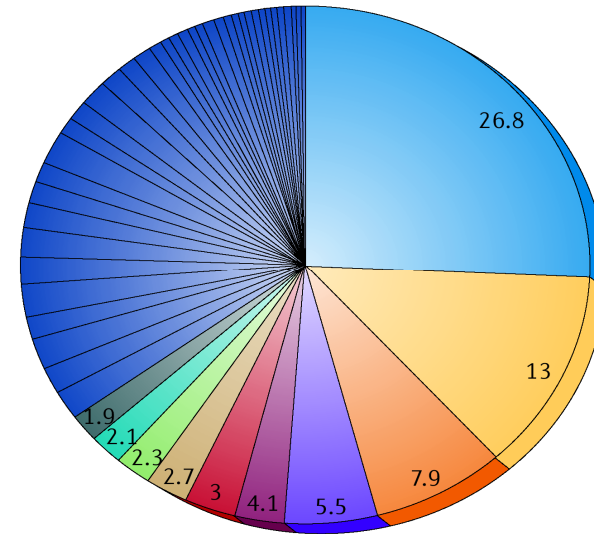
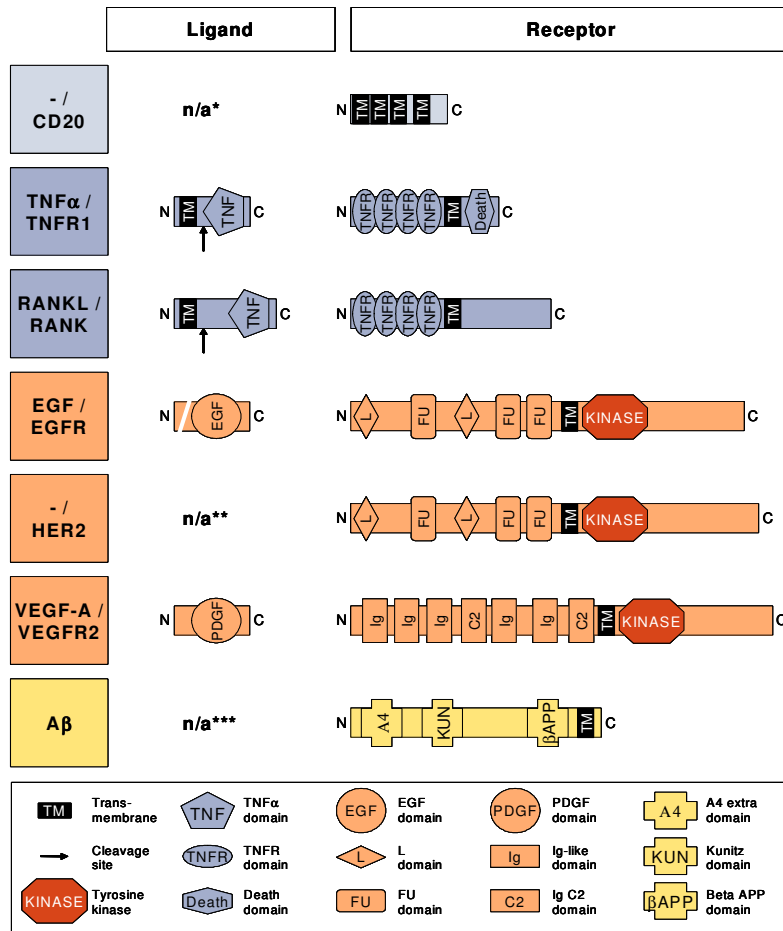
Molecular Targets For Antibody Drugs

Table 1 | **Molecular targets of FDA-approved drugs**

| Class of drug target | Species | Number of molecular targets |
|---|--------------------|-----------------------------|
| Targets of approved drugs | Pathogen and human | 324 |
| Human genome targets of approved drugs | Human | 266 |
| Targets of approved small-molecule drugs | Pathogen and human | 248 |
| Targets of approved small-molecule drugs | Human | 207 |
| Targets of approved oral small-molecule drugs | Pathogen and human | 227 |
| Targets of approved oral small-molecule drugs | Human | 186 |
| Targets of approved therapeutic antibodies | Human | 15 |
| Targets of approved biologicals | Pathogen and human | 76 |

Antibodies = 4.6%

Target Categories Mab vs NCE

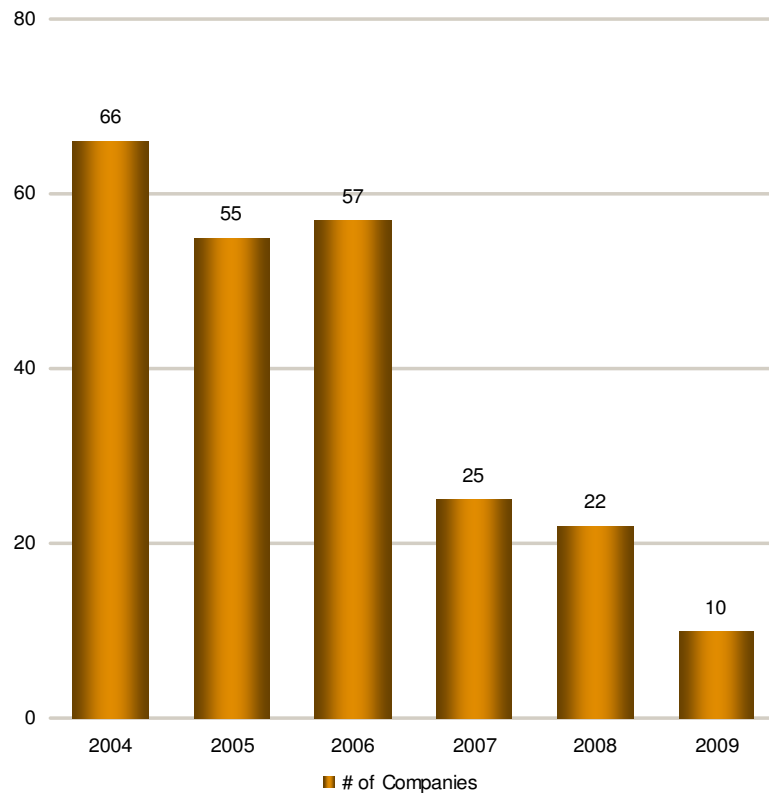


Summary

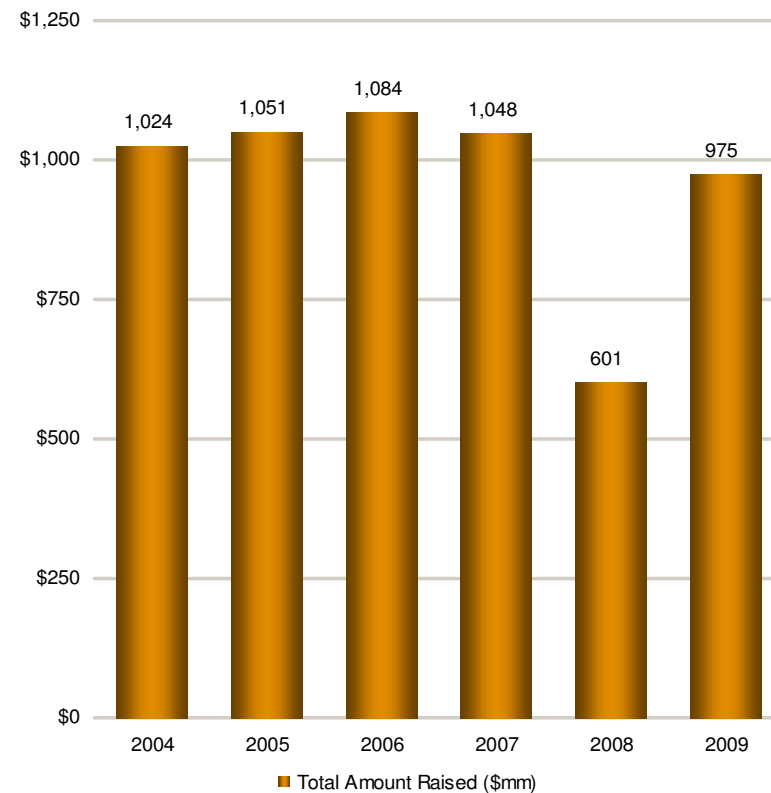
- Antibody/fragment drug discovery not technology limited
- Multiple routes to functionally equivalent molecules
- Pharma market growth is in secondary care
- Conventional Mabs will continue to dominate
- Short term growth driven by me-better & improveds
- Longer term horizontal expansion into new targets

The REAL challenge

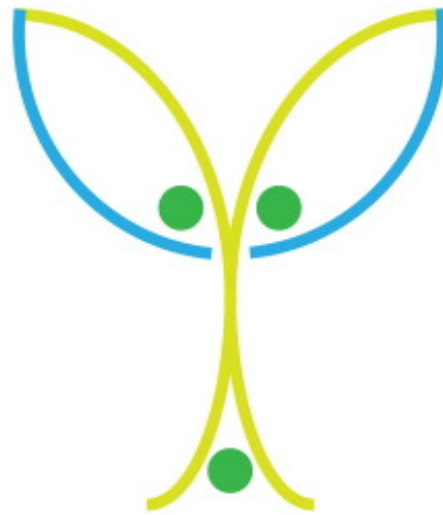
Number of New European Drug Development Companies Formed



Total Amount of Capital Raised For European Drug Development Companies



Source: CapIQ and Investment Analytics Report as of 12/15/2009.



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