Next Generation Protein Engineering and Drug Design

Strategies to improve drug efficacy and improve drug delivery

- Gain access to the product pipelines of your key competitors
- Exploit innovative protein engineering technology in your drug discovery process
- Forecast the protein engineering market to 2011
- Discover the range of tools available for engineering advanced protein drugs

New report from the Drug Discovery series...

Next Generation Protein Engineering and Drug Design

Strategies to improve drug efficacy and improve drug delivery

Report overview

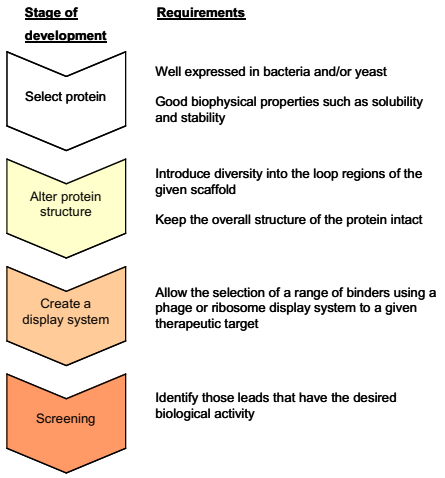
The success of protein and peptide therapeutics is revolutionizing the biotech and pharmaceutical market, spurring the creation of next-generation products with reduced immunogenicity, improved safety and greater effectiveness. New technologies and genetic and chemical techniques will ensure a competitive edge in developing improved protein and peptide based therapeutics.

Next Generation Protein Engineering and Drug Design provides a detailed insight into the current market for engineered proteins and peptides, and explores the key factors of commercial success for the development of next generation products. This report also provides in-depth analysis of patenting trends and market forecasts to 2011, enabling you to exploit innovative protein engineering technology in your drug discovery process.

Key findings

- The protein engineering market in 2006 was worth almost $67 billion, 10% of total pharma sales, and is forecast to rise to $118 billion, or 12% of pharma sales, in 2011.
- Oncology is the dominant therapy for both monoclonal antibodies and other types of engineered protein, accounting for one-third of sales overall and over 50% of all monoclonal antibodies.
- The top-selling therapeutic protein is Amgen's Aranesp, a re-engineered variant of the company's first-generation product, Epogen (recombinant human erythropoietin).
- Genentech has by far the most protein engineering-related US patents assigned to it (192, 7.4% of the total) and is the most frequently cited assignee, although over half its patents have never been referenced by subsequent US patent applicants.
- Enzon has licensed PEGylated half-life extension technology to Nektar Therapeutics and several refinements and proprietary approaches have recently been developed in this area.
- The last three years have seen the first approvals of products for nonparenteral delivery, alongside advances in parenteral protein and peptide drug delivery.

Figure 2.2: Protein scaffold used to create designer protein drugs



'Protein scaffolds can be used to create designer protein drugs. However, in many cases, the mutations introduced to enable binding to the target compromise the biophysical properties and/or the three-dimensional structure of the parental scaffold. In some cases, it may not even be possible to achieve the desired potency using such a small binding footprint to the given target...'

Next Generation Protein Engineering and Drug Design

Strategies to improve drug efficacy and improve drug delivery

Key questions answered

- What is the most dominant application for monoclonal antibodies and other types of engineered protein?
- Which companies have been most successful in targeting major clinical markets?
- Which company boasts the most prolific patenting in this area?
- How big is the therapeutic monoclonal antibody market?
- What types of monoclonal antibodies are under development?
- How will transgenic animal herds change the face of manufacturing complex therapeutic proteins?

Key issues examined in this report

- **Traditional protein therapeutics have many limitations.** In recent years a wide range of technologies has become available for use in protein engineering, which can be used to develop new versions of traditional products with improved characteristics.
- **Several antibodies on the market are directed against the same targets**. Increased competition is providing an impetus for the development of re-engineered, improved, whole antibody and antibody fragment-based products.
- **Immunogenicity is a problem, especially with antibodies**. The risk of immunogenicity can be reduced by using fully human recombinant antibodies or human antibodies derived from transgenic mice.
- **Patented therapeutic proteins stifle competition**. Chemical synthesis of medium-sized proteins is already possible enabling substantial protein re-engineering and may allow new products to be commercialized without risking patent infringement.
- **Several profitable protein therapeutics will soon come off-patent**. Engineered improvements would allow biosimilar products to be differentiated on the basis of superior characteristics.

Figure 1.1: US protein engineering patents and published applications by filing and publication years, 1992-2006

Year	By Date Filed No	%	Graph
Total	2604	100.0	
2006	74	2.8	
2005	153	5.9	
2004	102	3.9	
2003	148	5.7	
2002	179	6.9	
2001	287	11.0	
2000	237	9.1	
1999	258	9.9	
1998	193	7.4	
1997	175	6.7	
1996	136	5.2	
1995	369	14.2	
1994	182	7.0	
1993	81	3.1	
1992	30	1.2	

Year	By Date Published No	%	Graph
Total	2598	100.0	
2006	540	20.7	
2005	239	9.2	
2004	248	9.5	
2003	250	9.6	
2002	255	9.8	
2001	228	8.8	
2000	182	7.0	
1999	233	8.9	
1998	205	7.9	
1997	125	4.8	
1996	60	2.3	
1995	20	0.8	
1994	8	0.3	
1993	5	0.2	
1992	0	0.0	

Six patents were published in 2007.

'A patent application must disclose all relevant prior knowledge (or "prior art") on which the inventor has relied in developing his invention. In the absence of an agreement to the contrary (which is rare), patents awarded to employees of a company are generally assigned to that company and henceforth belong to it, although an owner can naturally sell or license his patent to others...'

Next Generation Protein Engineering and Drug Design

Strategies to improve drug efficacy and improve drug delivery

TABLE OF CONTENTS

CHAPTER 1: ENGINEERING NEXT GENERATION PROTEIN DRUGS

- Summary
- Introduction
- Background on proteins
- Patenting of proteins
- Regulatory requirements
- Commercial imperatives in protein engineering
- Introduction
- Application markets
- Manufacturer markets
- Product markets
- Geographical markets
- Patenting considerations
  - Usefulness of patent metrics
  - The protein engineering patent data set
- Analysis by assignee patent count
- Analysis by forward citation count
- Commercial outlook for engineered proteins

CHAPTER 2: STRATEGIES AND TECHNOLOGIES FOR PROTEIN ENGINEERING

- Summary
- Introduction
- Recombinant protein production
- Site-directed mutagenesis
- Post-translational modifications (PTMs)
- Glycosylation of natural proteins
- Manufacture of glycoproteins
- Glyco-remodeling
- Other PTMs
- Protein characterization
- Directed evolution
- Display technologies
- Use of protein scaffolds
- Peptide and protein synthesis
- Chemoselective ligation
- In silico protein design
- Technology-related patents
- Monoclonal antibodies
- Other proteins and peptides

CHAPTER 3: ENGINEERING IMPROVED MONOCLONAL ANTIBODIES

- Summary
- Natural antibodies
- Human IgG
- Generation of antibody diversity
- Monoclonal antibodies
- Evolution of mAbs
- Drivers for innovation
- The mAb business landscape
- Products on the US market
- Products in development
- Improving mAb production systems
- Cell lines
- Automation
- Manipulating mAb glycosylation profiles
- Enhancing mAb serum stability
- Engineering fully human mAbs
- Human mAbs from recombinant antibody libraries
  - Immune and nonimmune antibody libraries
  - Optimization
  - Phage display libraries
  - Ribosome and mRNA display antibodies
  - Yeast-display antibodies
- Human mAbs from transgenic mice and chickens
- Human mAbs on the market and in development
- Engineering novel antibody fragments
- Monovalent fragments
- Multivalent fragments
- Fragments on the market and in development
- Engineering for specific therapeutic applications
- Cancer
  - Unconjugated mAbs
  - Conjugated mAbs and fusion proteins
- Immune and inflammatory disorders
- Other areas

CHAPTER 4: ENGINEERING ALTERNATIVES TO ANTIBODIES

- Summary
- Introduction
- Comparison with monoclonal antibodies
- Combinatorial scaffold libraries
- Scaffolds used in library construction
  - Beta-sheet frameworks
  - Mixed/irregular secondary structures
  - Alpha-helical frameworks

  - Repeat proteins
- Scaffold optimization and diversification
- Selection technologies
• Recognition proteins as therapeutics
- Products in commercial development
  - Adnexus Therapeutics
  - Evogenix
  - Bristol Myers-Squibb
  - Pieris Proteolab
  - Avidex
  - Affibody
  - Molecular Partners
  - Aptanomics
  - Selecore
  - Avidia
  - BioRexis
  - Isogenica
  - Bracco Research

CHAPTER 5: ENGINEERING OTHER PROTEIN AND PEPTIDE DRUGS

• Summary
• Introduction to protein/peptide drugs
- Drivers for innovation
• The business landscape
- Products on the market and in development
• Improving production systems
- Recombinant methods
- Transgenic methods
- Chemical methods
- Tackling immunogenicity
• Manipulating PTMs
- Glycoprotein profiling
- Glyco-engineering
  - Amgen
  - Genzyme
  - Neose Technologies
  - University of Maryland
- Other PTMs
• Altering plasma half-lives
- Amino acid modifications
- Variations in glycosylation
- PEGylation
- Chemical modification
- Other novel approaches
- Case study: Erythropoiesis-stimulating agents
• Expediting peptide drug discovery
- Phage and other display technologies
  - Dyax
  - California Institute of Technology
- Rational design
  - Peptide mimetics
- Case study: Antimicrobial peptide discovery
• Exploring the role of pharmacogenomics

CHAPTER 6: ENGINEERING PROTEIN THERAPIES FOR DELIVERY

• Summary
• Introduction
• Injectable protein delivery
- Half-life extension technologies
  - PolyTherics' TheraPEG PEGylation technology
  - Affymaxs' PEGitecture technology
  - Neose Technologies' GlycoPEGylation technology
  - Approved PEGylated biopharmaceuticals
  - Other approaches
- Depot systems
  - Biodegradable drug carrier systems
  - Microsphere-based delivery systems
  - Nanoparticle dispersions
  - Drug release mechanisms
• Pulmonary delivery
- Exubera (inhalable recombinant insulin)
- Alkermes' AIR dry powder
- Aradigm's AERx system
- Baxter Healthcare's Promaxx technology
- Syntonix Pharmaceuticals' Fc Fusion Proteins
• Nasal delivery
• Oral and other forms of delivery
- Cell penetrating peptides and polymeric nanoparticles
  - Emisphere's Eligen technology
  - Merrion Pharmaceuticals' GIPET
  - Nobex's drug delivery technology
  - Mucoadhesive polymer technologies
  - Nautilus Biotech
• Other approaches
  - Affinergy
  - Raptor Pharmaceutical

CHAPTER 7: TRENDS AND OPPORTUNITIES

• Creating non-immunogenic monoclonal antibodies
• The next wave of monoclonal antibody-based agents
• Beyond monoclonal antibodies
• The challenge of follow-on biologics
• The promise of synthetic peptides and proteins
• New frontier: de novo protein design

Business Insights

FAX BACK TO: **+44 (0) 207 900 6688**

or scan and e-mail to

marketing@globalbusinessinsights.com

1 I would like to order the following report...

(Please use BLOCK CAPITALS)

_____

_____

☐ **Hard Copy** (extra £50/€75/$95)
Please allow 28 days for delivery

☐ **Interactivity** (extra £50/€75/$95)
Search, customize & translate content

2 Please select a license type:

	GB£	EUR€	US$
☐ **Single User (eCopy)**	1995	2880	3835
Access permitted for one individual only			
☐ **Site License**	3790	5470	7285
Access permitted for every individual based at one location			
☐ **Company License**	7475	9180	12180
Global access for every individual member of staff at the company			

To ask a question about license types, email: **marketing@globalbusinessinsights.com**

Communications Feedback

Please let us know if any of the following factors influenced your purchase...

- ☐ Email/Fax/Postal promotion
- ☐ Brochure
- ☐ Table of Contents
- ☐ Colleague Recommendation
- ☐ Trade Press
- ☐ My Account Manager
- ☐ Conference materials
- ☐ Website/web search

Recipient details *(If different from Payor)*

Title: Mr/Mrs/Ms **(Please use BLOCK CAPITALS)**

First Name: Last Name:

Email

Job Title

Department

Address

City State/Province

Country Post Code/ZIP

Tel Fax

3 Company details

Company name: _____

EU companies (except UK) must supply VAT / BTW / MOMS / MWST / IVA / FPA number:

_____

Purchase Order Number (if required)_____

4 Payment method

Please indicate your preferred currency: ☐ GB£ ☐ EUR€ ☐ US$

Total order value is _____

- ☐ I will forward a check payable to Business Insights Limited.
- ☐ Please invoice my company (please complete invoice address below)
- ☐ I would like to pay by bank transfer (email address required)
- ☐ Debit my credit/charge card: Amex Visa Mastercard

Card No_____

Expiry Date _____/_____ Signature _____

5 Payor details

Title: Mr/Mrs/Ms **(Please use BLOCK CAPITALS)**

First Name: Last Name:

Email

Job Title

Department

Address

City State/Province

Country Post Code/ZIP

Tel

Fax

Sign here to confirm your order:

ORDERS WITHOUT A SIGNATURE CANNOT BE PROCESSED

Marketing Department
marketing@globalbusinessinsights.com

Code Ref: Website

www.globalbusinessinsights.com

+44 (0) 20 7551 9700

Registered Office: Business Insights Ltd, Mortimer House, 37-41 Mortimer Street, London W1T 3JH.
UK Registered Number: 05006037