Associazione Culturale G. Dossetti

FARMACI INNOVATIVI

Giovedì 26 Giugno 2008

Camera dei Deputati

Palazzo Marini, Sala delle Conferenze

La Biotecnologia può migliorare la nostra Vita ?

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Biotechnology is changing the world

The Birth of Biotechnology

In 1973, Herbert Boyer and Stanley Cohen reported that a mammalian gene was cloned and expressed in bacteria and produced a viable protein

Recombinant DNA technologies established the "Biotechnology Revolution" by providing abundant sources of proteins of practical interest

PROTEINS GOVERN

ALL THE PROCESSES OF

LIVING ORGANISMS

Proteins are made by 20 amino acids

- Dipeptides (*e.g.*, Gly-Ala, Ala-Gly, Phe-Ala, Ala-Phe,... are 20 X 20 = 400
- Tripeptides are 20 X 20 X 20 = 8000
- Tetrapeptides are 20 X 20 X 20 x 20 = 160.000
- Decapeptides are 10.000 billions
- Proteins of 100-200 amino acids are... infinite

PROTEINS IN THE CELL

A VERY CROWDED ENVIRONMENT

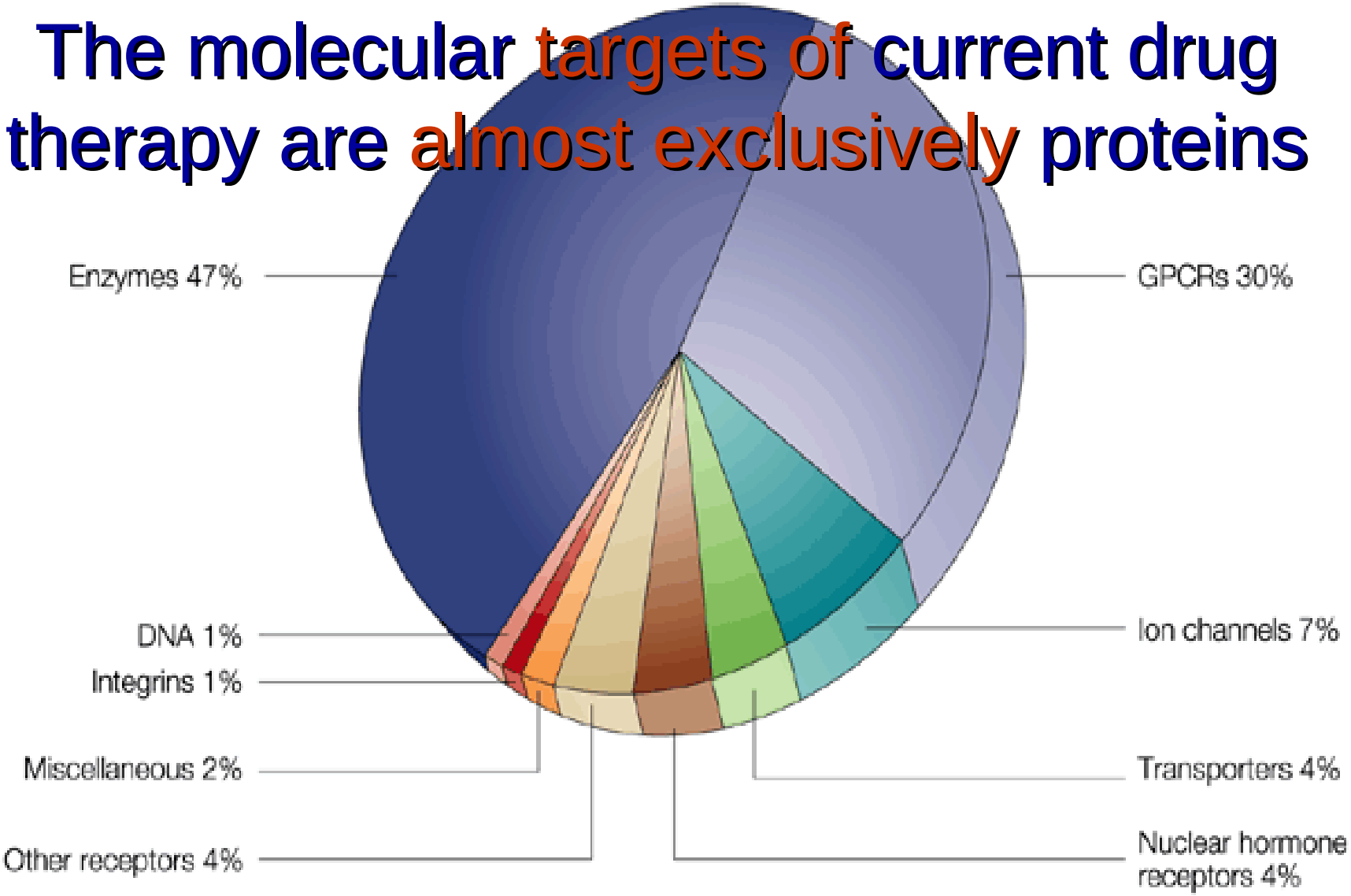
200-300 mgs protein per ml

DRUG THERAPY

All known drugs have been listed according to their molecular mechanism of action.

Current drug therapy is based on some 500 molecular targets.

The molecular targets of current drug therapy are almost exclusively proteins



Hopkins, A.L. and Groom, C.R. (2002) *Nature Rev. Drug Disc. 1*, 727-730.

PROTEINS are the key players in drug action

- Small molecule, synthetic drugs act almost exclusively on proteins

- Protein drugs are the products of biotechnology

The (Major) Products of Biotechnology

Insulin, Calcitonin, Somatostatin,
Glucagon, FSH, TSH, Factor IX, DNase,
Factor VIII, Hirudin, hGH, EPO,
CSF, Interferons, Interleukins,
TPA, Antibodies, Recombinant vaccines

Protein Drug Milestones

Human insulin

First application of biotech in medicine

Recombinant human growth hormone

First biotech human growth hormone with no risk of CJD infection

Recombinant interferon–beta

Enabled real progress in treating multiple sclerosis

Recombinant erythropoietin (EPO)

Revolutionized the treatment of anemia, eliminating viral infections including AIDS and hepatitis B or C

Monoclonal antibodies for the treatment of cancer

Development of drugs targeting specific types of cancer cells: Herceptin (*Trastuzumab*) for breast cancer

Healthcare biotechnology is saving lives, helping patients and serving society.

Diseases that can be cured by protein drugs

Cancer

Cardiovascular Diseases

Diabetes

Growth Hormone Deficiency

Haemophilia

Hepatitis B

Inflammatory Diseases

Multiple Sclerosis

Anemia

A recent Report from the Pharmaceutical Research and Manufacturers of America (PhRMA) found 418 protein drugs developed through biotechnology) now being tested to treat more than 100 diseases. All of them are now in clinical trails or awaiting approval from the US Food and Drug Administration (FDA).

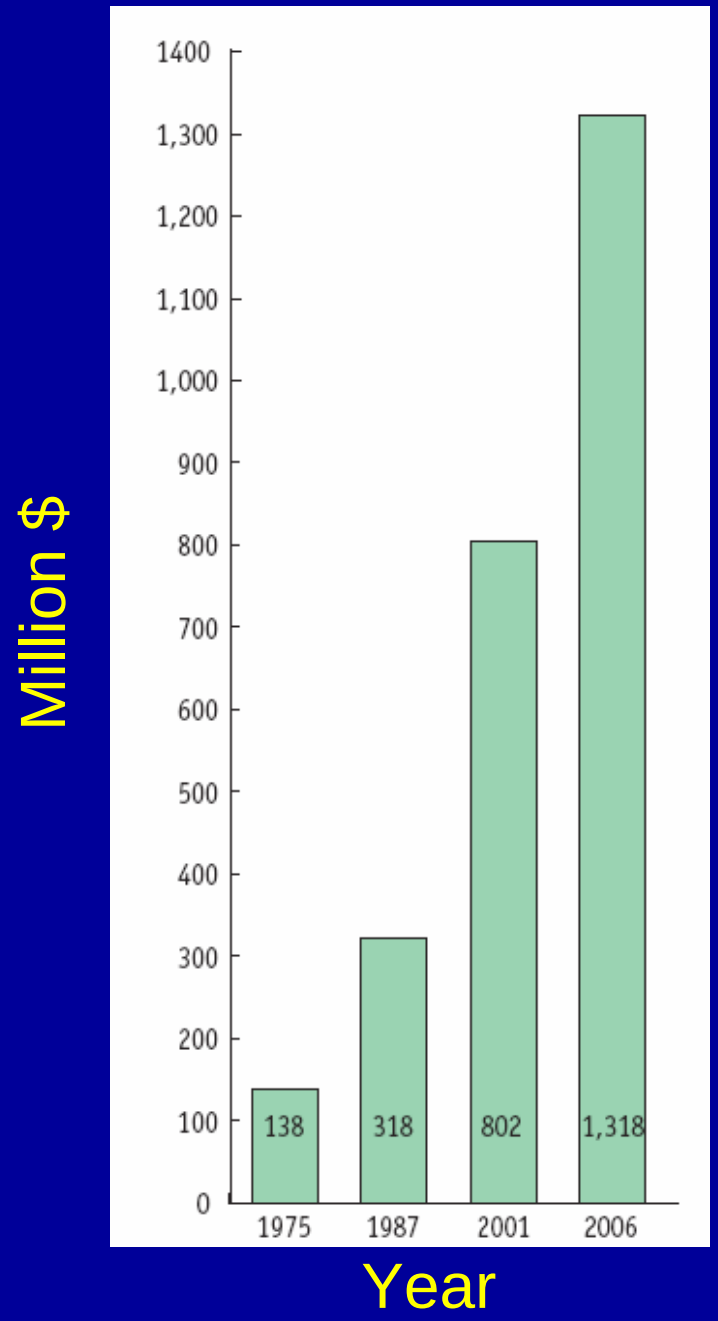
Among these 418 biotech drugs, there are

- 210 to treat cancer
- 50 to treat infectious disease
- 44 to treat autoimmune disorders
- 22 to treat HIV infection
- 22 to treat cardiovascular diseases

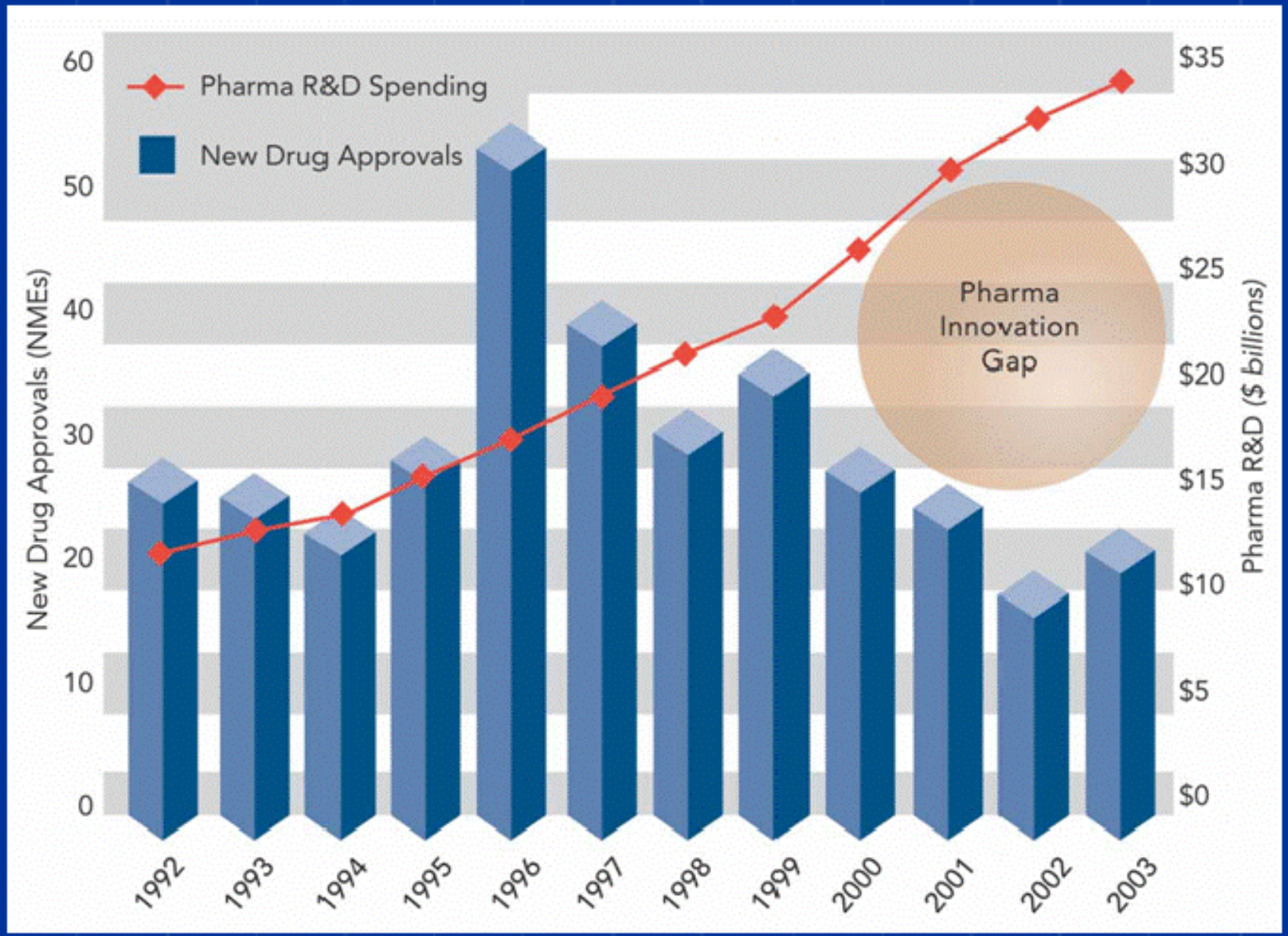
Protein Drugs are Costly !

Market Forecasts for Leading Protein Drugs ($ millions)

Product class	2003	2004	2005	2006	2007	2008	2009
Erythropoietins	7,763	8,136	8,473	9,268	9,777	10,893	11,779
Monoclonal antibodies	6,721	11,079	13,986	17,734	20,599	36,399	45,352
Insulin and insulin analogues	5,487	6,551	7,940	9,236	10,772	13,828	17,363
Interferons	3,935	3,692	3,825	4,050	4,392	4,983	5,828
Therapeutic hormones (including growth hormones)	3,317	3,895	4,186	4,280	4,456	4,990	5,799
Blood factors	2,354	2,598	2,595	2,679	2,998	3,215	3,432
Enzyme replacement therapies	1,057	1,203	1,374	1,533	1,713	2,111	2,738
Interleukins	219	224	229	237	250	260	273
Other therapeutic hormones	121	111	72	212	520	1,595	2,514
Total	**30,974**	**37,489**	**42,680**	**49,229**	**55,477**	**78,274**	**95,078**



Estimated Total Cost
of Bringing a
New Drug to Market


Pharma R&D Spending
New Drug Approvals
Pharma Innovation Gap
New Drug Approvals (NMEs)
Pharma R&D ($ billions)
0
10
20
30
40
50
60
$0
$5
$10
$15
$20
$25
$30
$35
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003

Biogenerics
Biosimilar
Drugs

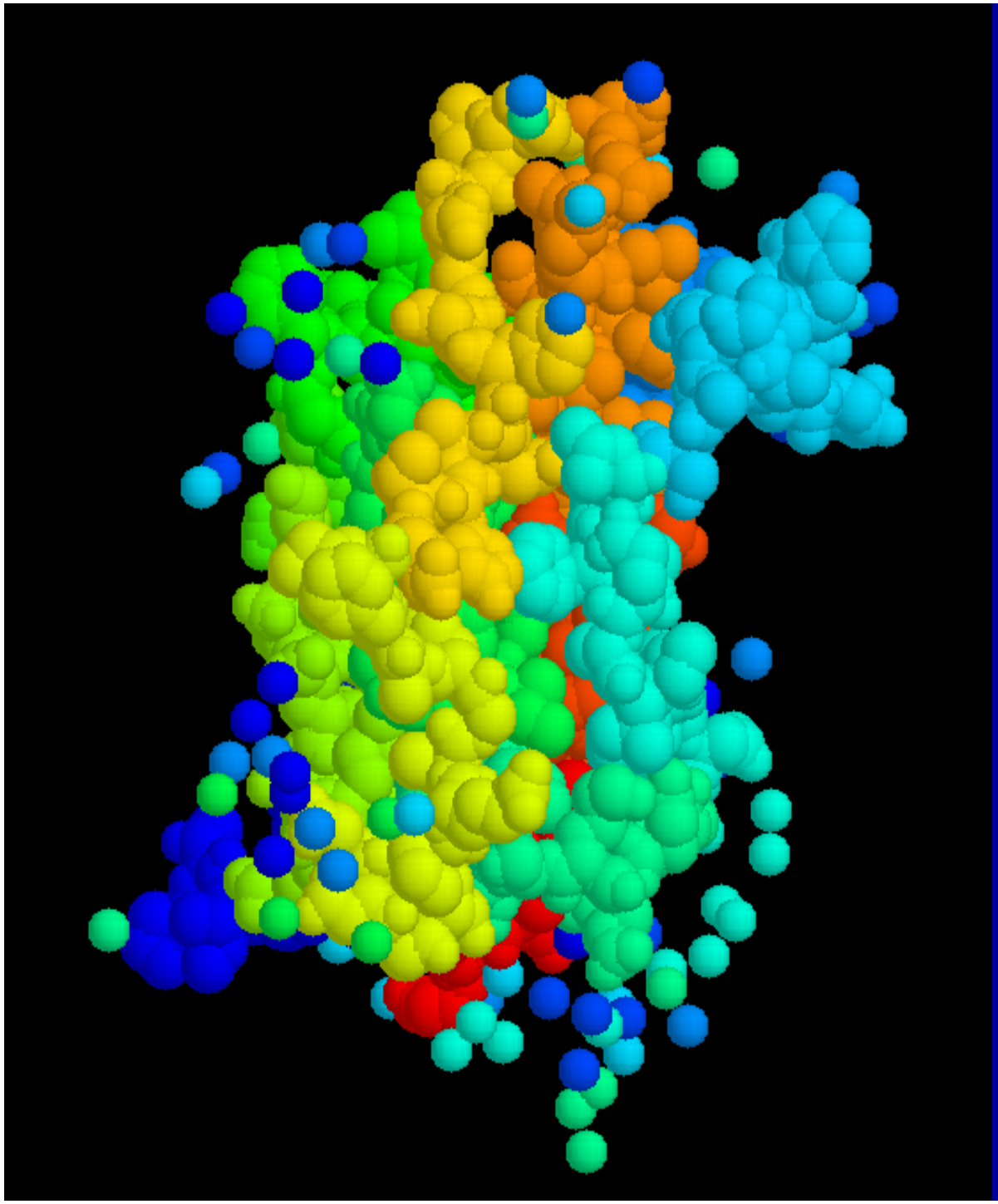
BIOGENERICS

- Due to the high cost of medical treatment using biotech drugs, there is considerable incentive to develop low-cost generic forms of the original protein drugs. This trend in biotechnology raises new opportunities for bioindustries.

- However, nowadays a strong debate is occurring regarding the bio-equivalence between protein drugs due to their inherent molecular and functional complexity.

- There remains a strong requirement to conduct clinical development similar to those for original products, which in effect results in high development cost and lengthy research and development (R&D) timelines for small bioindustries.

PROTEINS ARE DIFFICULT !



Space-filling model of growth hormone

How complex, but beautiful, are protein molecules!

The highway to protein drugs

- Gene identification
- Cloning
- Fermentation technology
- Downstream processing
- Bioseparation technology
- Protein chemistry
- Mass spectrometry
- Biospectroscopy
- X-Ray crystallography
- Bioinformatics
- Immunochemical techniques
- Protein stability and stabilization
- Protein formulation and delivery

DRUG DISCOVERY

Before DNA

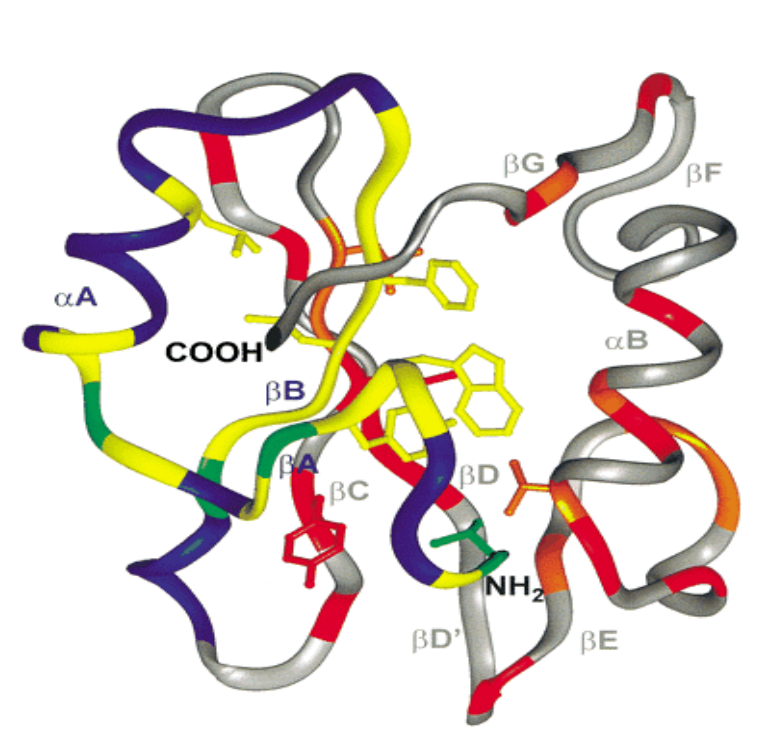
Driven by Chemistry and guided by Pharmacology and Clinical Sciences.

After DNA

Molecular Biology, Genomics, Proteomics and Bioinformatics play a most critical role in the pipeline to new drugs.

In the third millennium...

A variety of research areas, approaches and techniques is required for drug discovery within the Pharmaceutical Industry

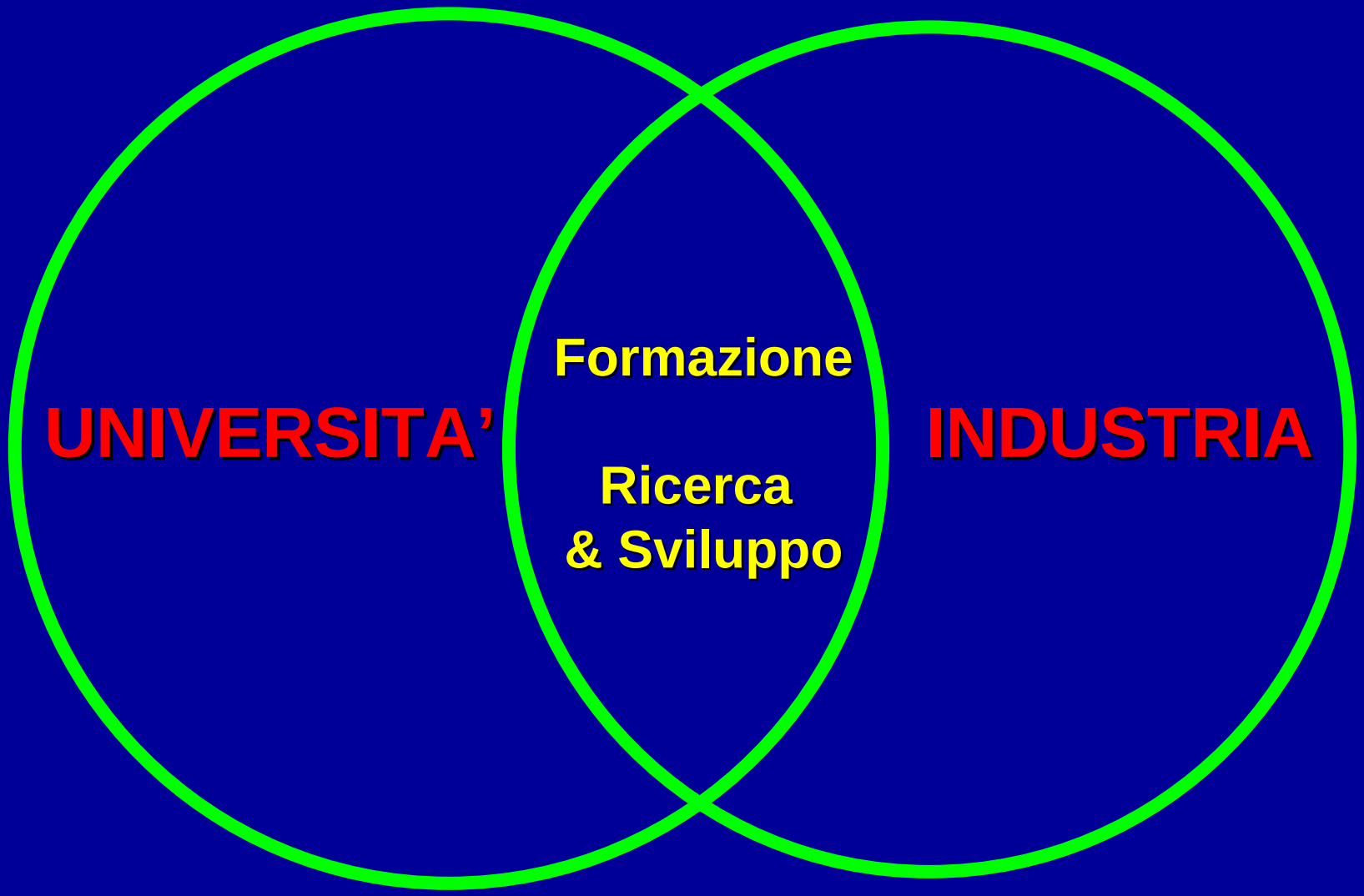


- . Genomics
- · Structural Biology
- · New Technologies
- · Proteomics
- · Protein Biochemistry
- · Discovery Biology
- · Functional Genomics
- · Molecular Biology
- · Developmental Biology
- · Genetics
- · *In silico* Biology
- · Pharmacology
- · Pharmacogenomics
- · Bioinformatics
- · Molecular Diagnostics
- · Toxicology
- · Chemoinformatics
- · Screening
- · Preclinical Development
- · Product Development

A solid scientific infrastructure is required for the development of

Industrial Biotechnology

in Italy


UNIVERSITA'
Formazione
Ricerca
& Sviluppo
INDUSTRIA

BIOTECNOLOGIE FARMACEUTICHE

PROTEIN DRUGS

ENABLING EXPERTISES AND TECHNOLOGIES

MOLECULAR BIOLOGY
GENETICS
MICROBIOLOGY
BIOCHEMISTRY

PROTEIN CHEMISTRY
BIOSEPARATIONS
MASS SPECTROMETRY
BIOSPECTROSCOPY

PROTEIN STABILITY
AND STABILIZATION
PROTEIN FORMULATION
AND DELIVERY

INNOVATIVE MEDICINES INITIATIVE

BETTER TOOLS
FOR BETTER MEDICINES

"This initiative has the potential to provide a quantum leap in the efficiency of the drug development process. It is an ideal vehicle for strengthening Europe's position as a centre of excellence in biopharmaceutical R&D. The methods and knowledge generated by IMI will greatly benefit society by accelerating the development of better medicines for diseases affecting millions of patients in Europe and worldwide. We are proud to be partners in this historic public-private collaboration."