

Council for Mineral Technology



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metallurgical innovation

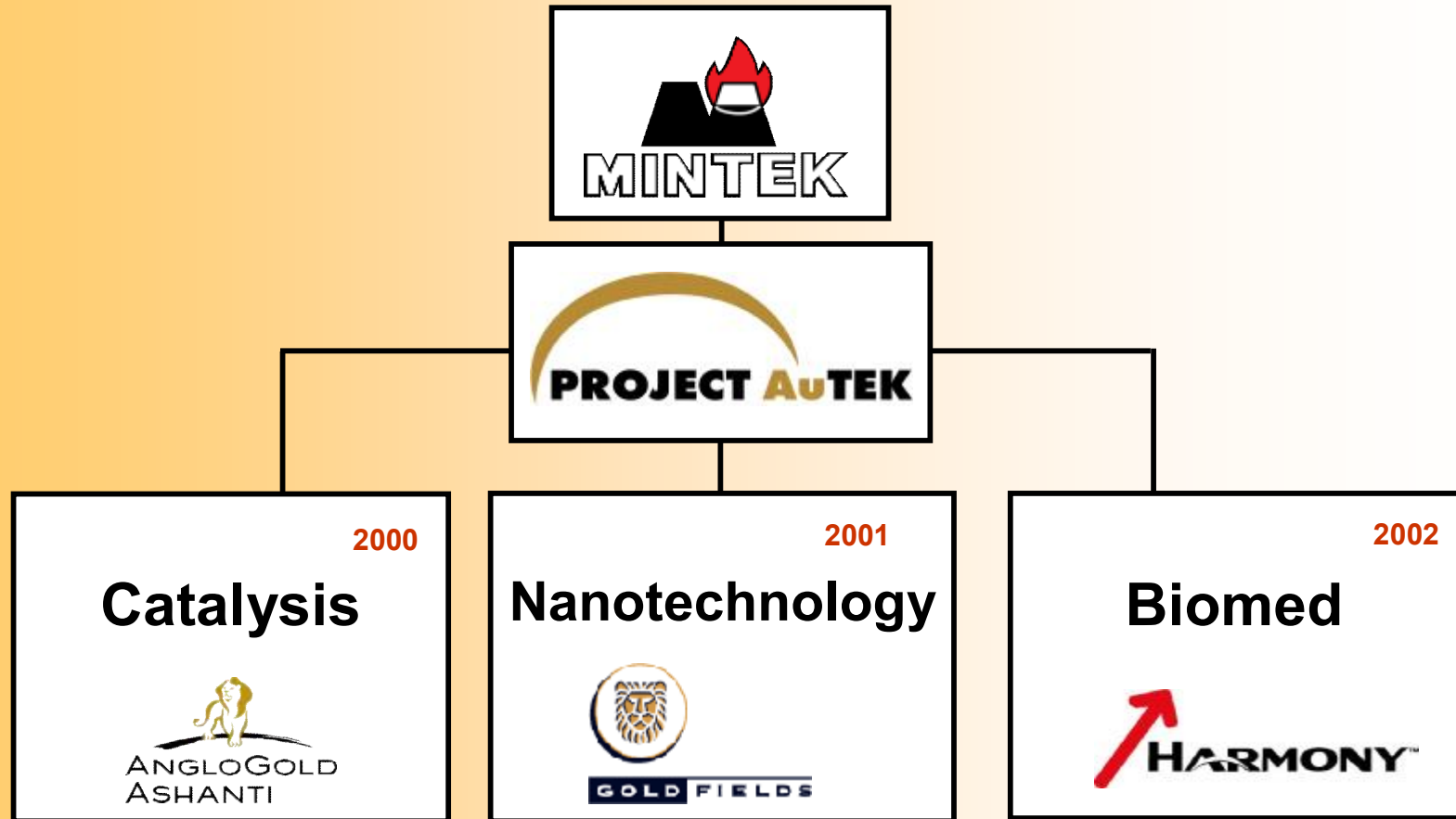
AuTEK Biomed: The Biomedical Applications of Gold

Raymond Hewer

5 June 2009



AuTEK





- Investigations into the Biomedical Applications of gold
- Basic research into early stage drug discovery
- Focused on HIV, Malaria and Cancer
- Identifying gold-based compounds that have the potential to be developed into anti-cancer, anti-malaria or anti-HIV agents

HIV in South Africa

HIV prevalence in 2007: 28%

AIDS related deaths in 2006: 605,480

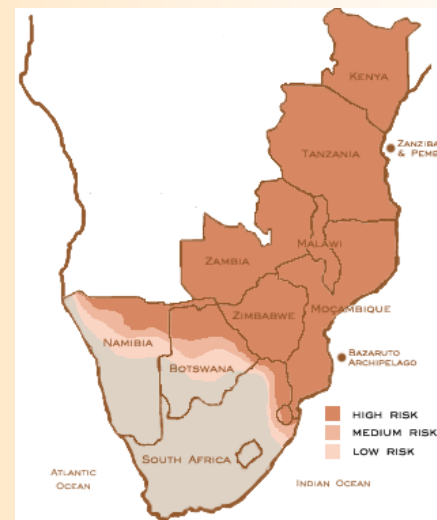
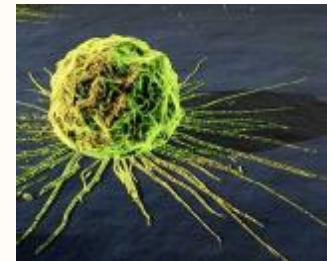
Cancer in South Africa

An estimated 1 in 4 persons will develop cancer

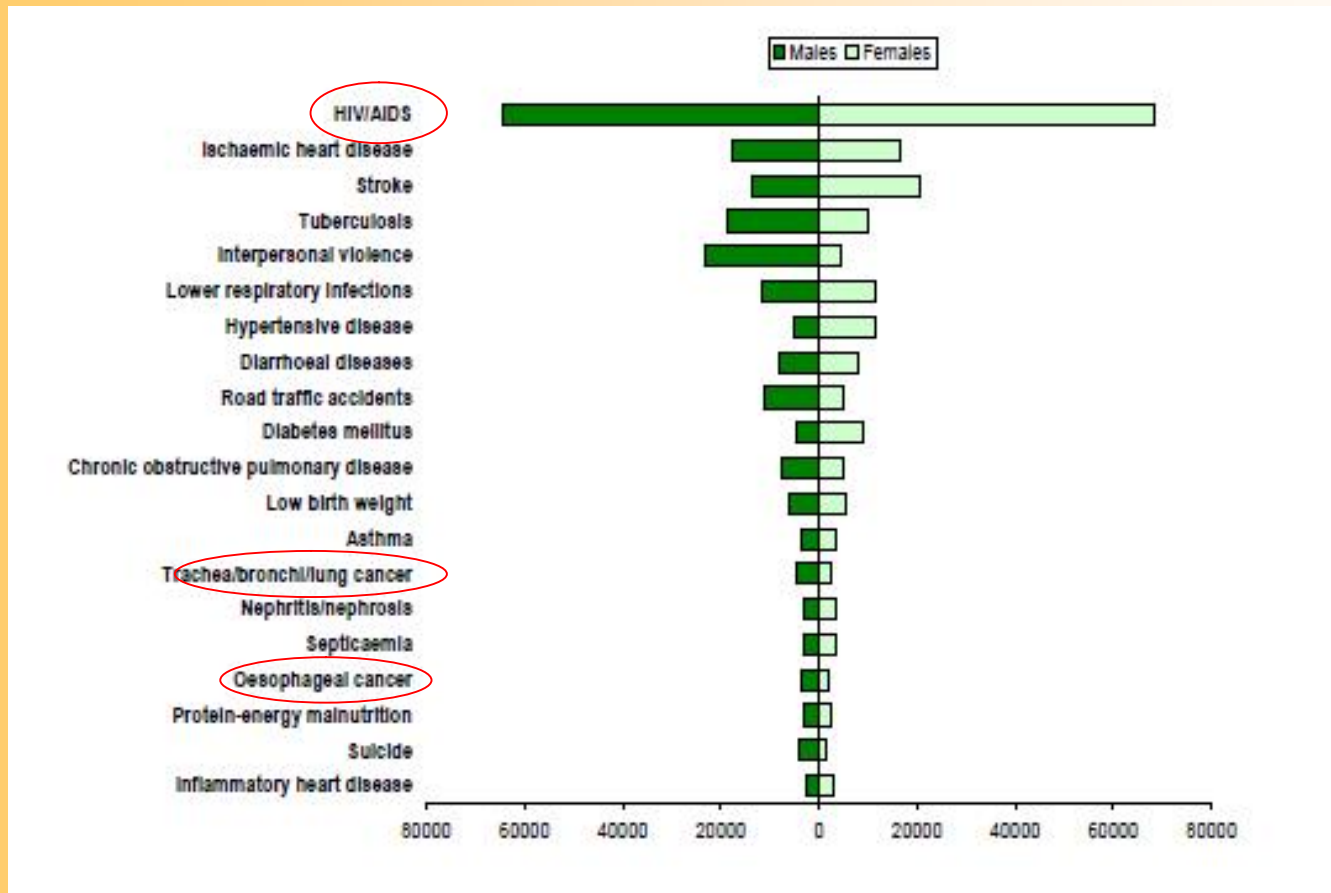
Malaria in South Africa

+/- 7000 cases reported yearly

Over 60 000 cases reported in 2000



Disease burden in South Africa



Rosana Norman, Debbie Bradshaw, Michelle Schneider, Desiree Pieterse and Pam Groenewald. **Revised Burden of Disease Estimates for the Comparative Risk Factor Assessment, South Africa 2000**

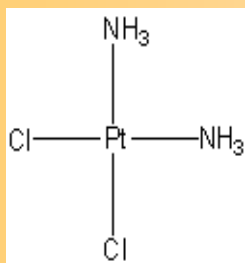
Metals in Medicine

- Metals in medicine dates back to earliest recorded history
- Medicinal use of gold traced back to 2500BC in China
- Egyptians used copper to sterilise water
- Early 20th Century
 - gold cyanide treatment for tuberculosis
 - antimony for the parasite, Leishmania
 - treatment of rheumatoid arthritis – sodium aurothiomalate and aurothioglucose
- Followed by the orally bioavailable Auranofin in 1985

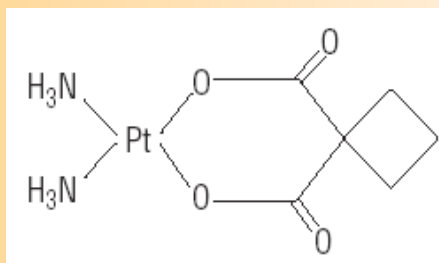


Metals in Medicine

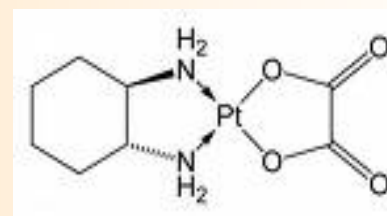
- Magnesium, aluminium oxides, calcium carbonate, bismuth subsalicylate – over the counter
- Lithium carbonate and sodium nitroprusside
- Serendipitous discovery of platinum drug, cisplatin
- Launched the search for improved platinum-based therapies and alternative metals for new therapeutic uses



Cisplatin



Carboplatin



Oxaliplatin

AuTEK BIOMED

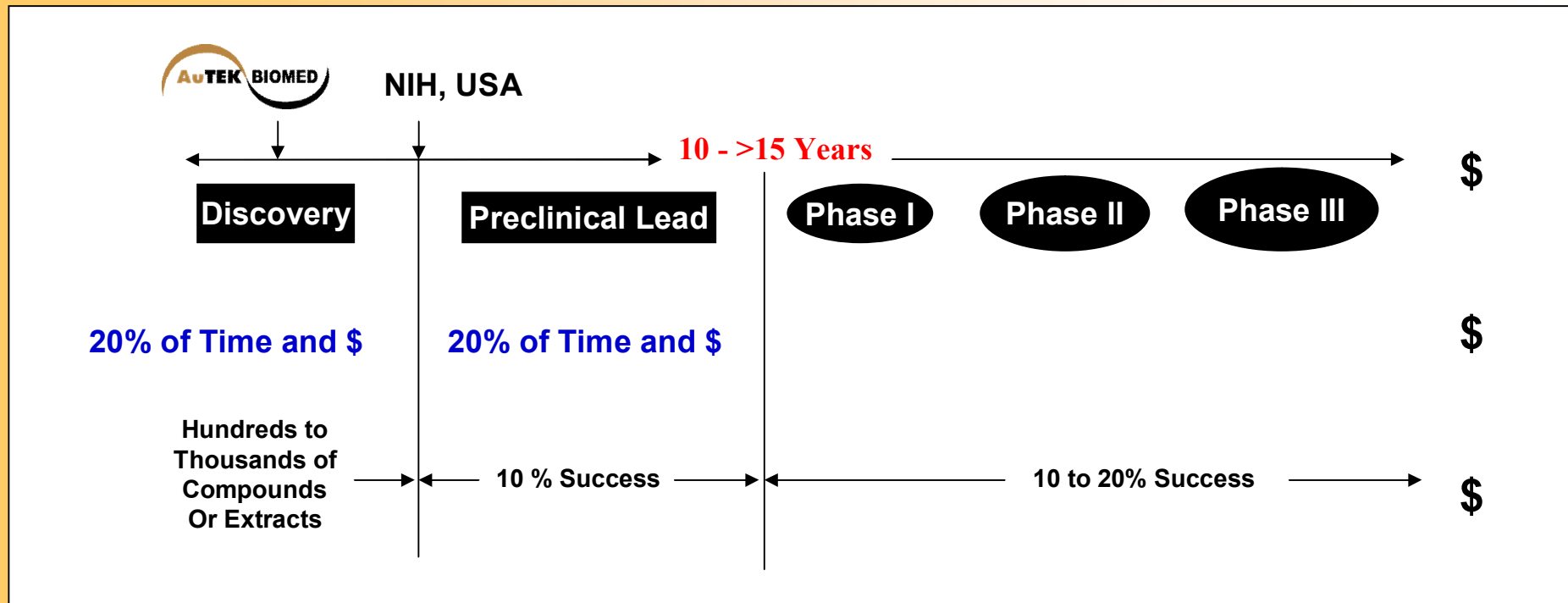
AuTEK Biomed: Early stage drug discovery in the field of:

HIV

Mintek and University-based program

Malaria and cancer

University-based programs



AuTEK BIOMED

Local:

Universities

Cape Town

Johannesburg

KwaZuluNatal

Pretoria

Western Cape

Witwatersrand

Platforms

NECSA

CANSA

SAMI

PCDDP

CBT

SARIMA

International:

Universities

University of Sassari, Italy

University of Lund, Sweden

Emory University, USA

Institutions

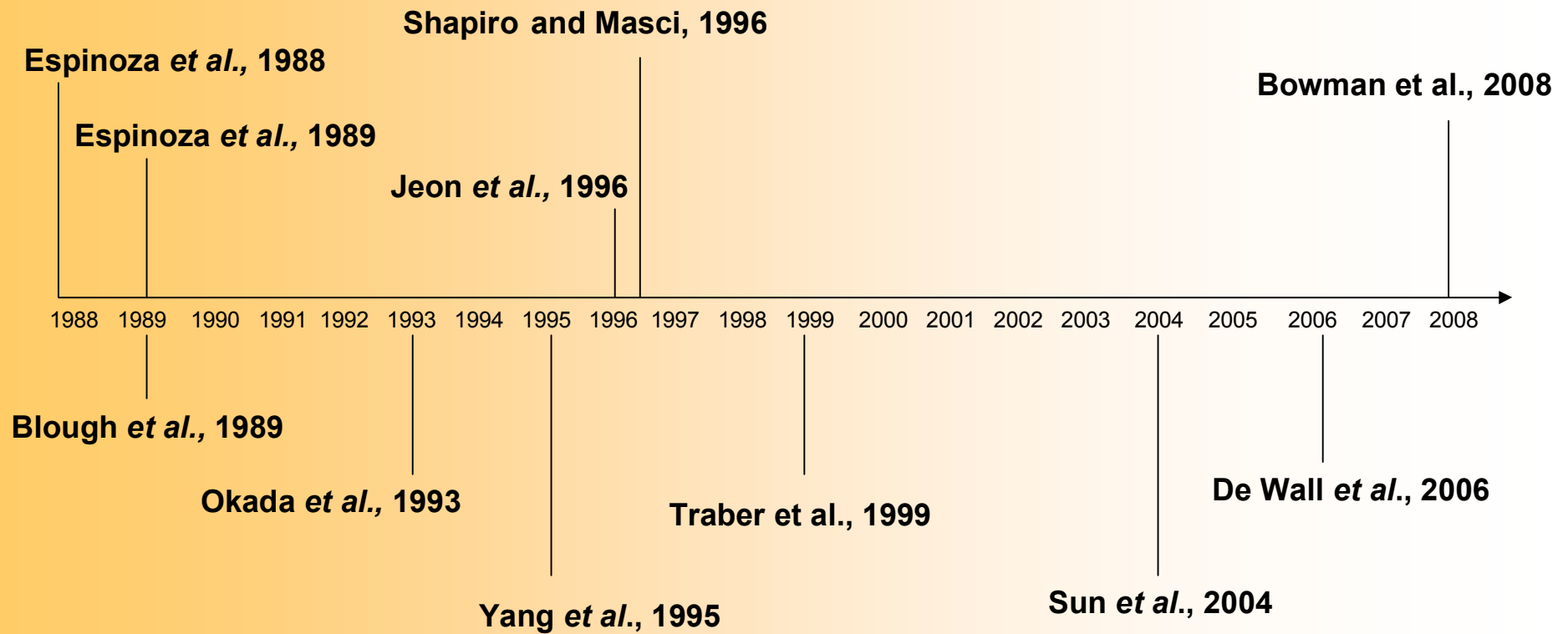
NIH, USA

COST, EU

Industrial Partner



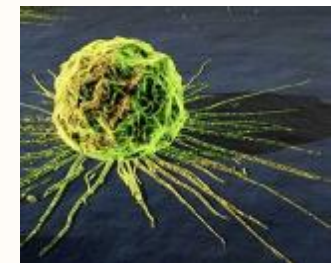
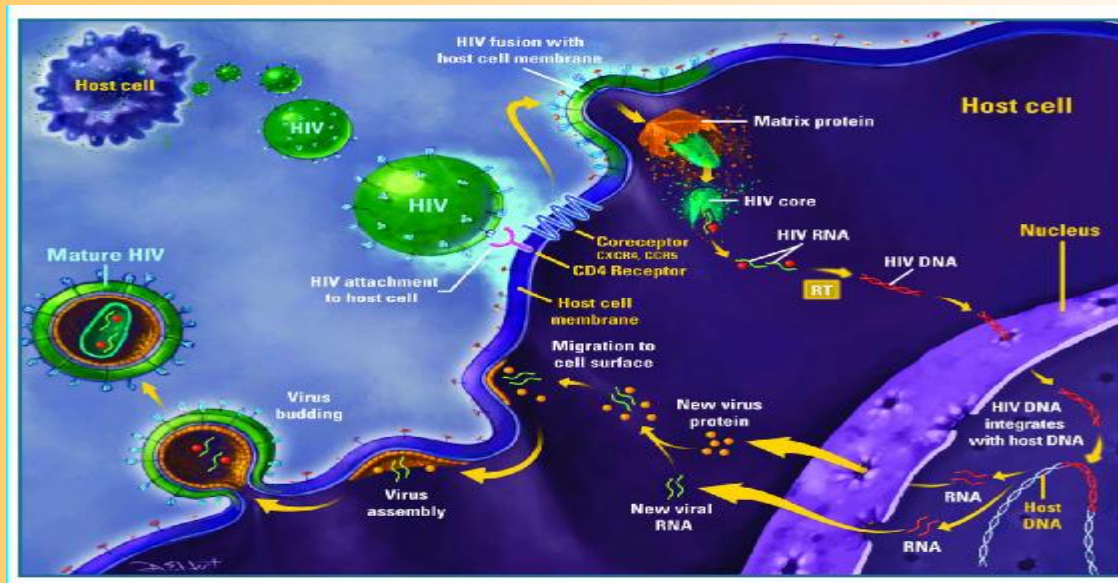
Identifying gold-based anti-HIV agents



Identifying gold-based anti-HIV agents

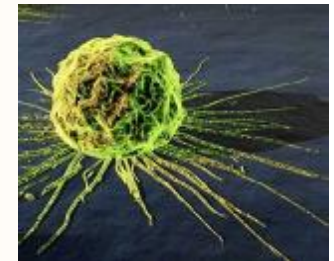
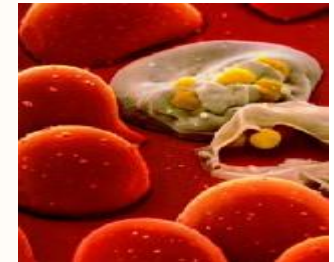
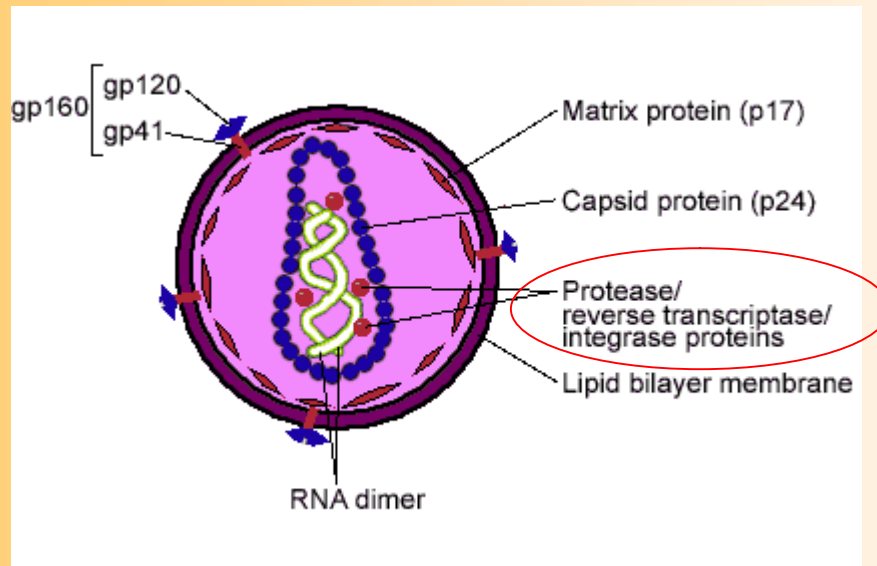
1. Rational design of gold compounds

- Target vital factors in the HIV lifecycle



Identifying gold-based anti-HIV agents

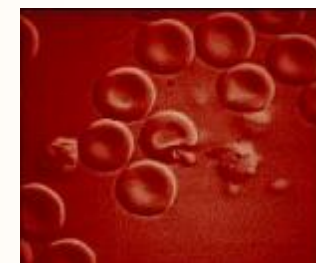
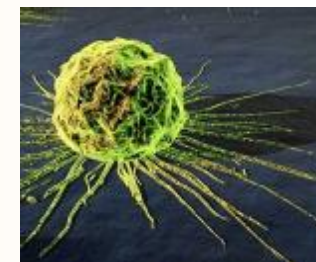
1. Rational design of gold compounds
 - Target vital factors in the HIV lifecycle



Identifying gold-based anti-HIV agents

1. Rational design of gold compounds

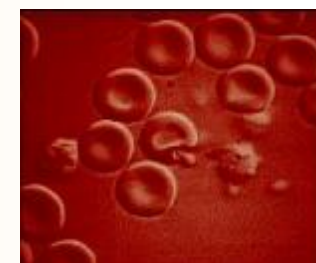
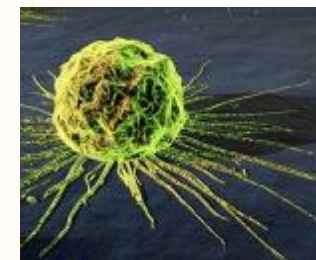
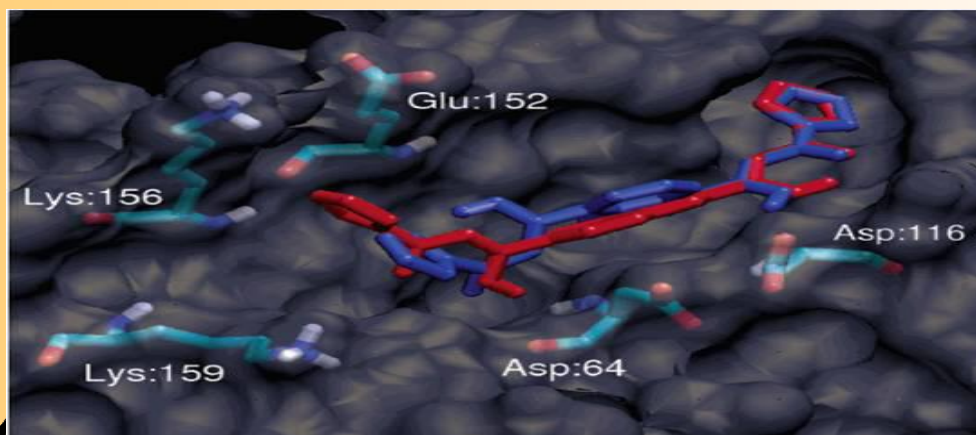
- Target vital factors in the HIV lifecycle
 - reverse transcriptase
 - protease
 - integrase
- Molecular models of HIV enzymes



Identifying gold-based anti-HIV agents

1. Rational design of gold compounds

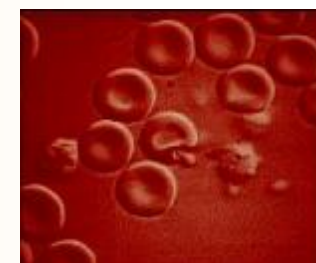
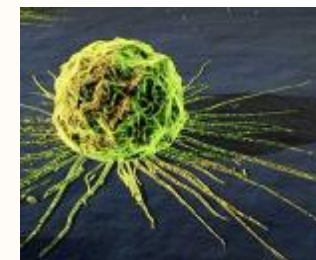
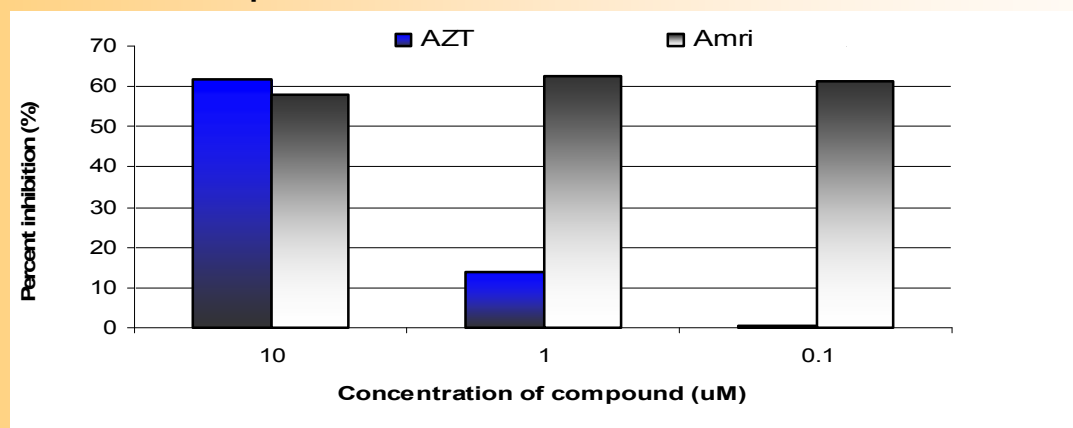
- Target vital factors in the HIV lifecycle
 - reverse transcriptase
 - protease
 - integrase
- Molecular models of HIV enzymes
- Focus on the active site



Identifying gold-based anti-HIV agents

1. Rational design of gold compounds

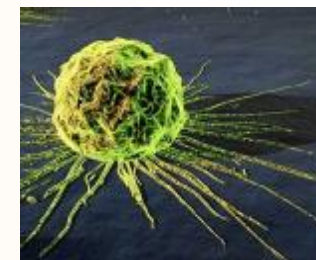
- Design compounds with high binding affinity to active site
- Synthesise a family of related compounds
- Evaluate these compounds in biological assays
- Results as to date:
 - Identified 59 compounds with high docking scores
 - 1 HIT compound



Identifying gold-based anti-HIV agents

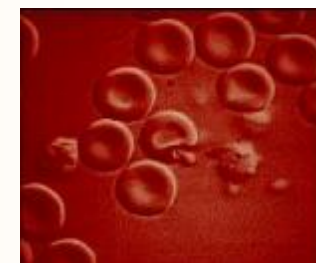
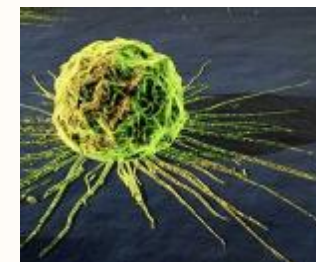
2. The traditional “Shotgun” approach

- Screen a library of compounds in various biological assays
- Gold-compound library of >400 compounds
- Screened 150 compounds in biological assays
- Results as to date
 - 7 HIT compounds with significant anti-HIV activity
 - Suffer from high toxicity and low selectivity
 - Toxicity not a general problem
 - Gold-compounds demonstrate high solubility
 - Gold-compounds are drug-like



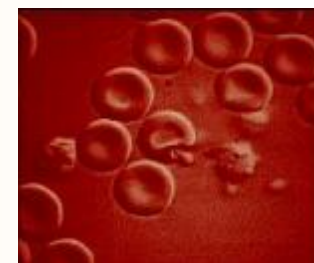
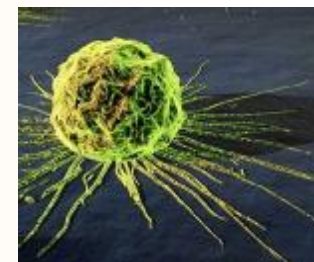
Identifying gold-based anti-cancer and anti-malarial agents

- University based projects
- Malaria primary findings:
 - “Shotgun” approach with >50 compounds screened
 - Comparative studies have shown clear evidence of the benefit of gold
- Cancer primary findings:
 - “shotgun” approach with >200 compounds screened
 - 14 HITS identified for further development (NIH, USA)
 - 2 LEAD compounds generated
 - 1 compound remains in the pipeline



Summary

- The use of metals in medicine is extensive
- The biomedical application of gold-based drugs has been established
- Findings from AuTEK Biomed further substantiate the potential of developing gold-based anti-HIV, anti-cancer or anti-malarial compounds



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NIADS

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NRF