

# Council for Mineral Technology



A global leader in mineral and  
metallurgical innovation

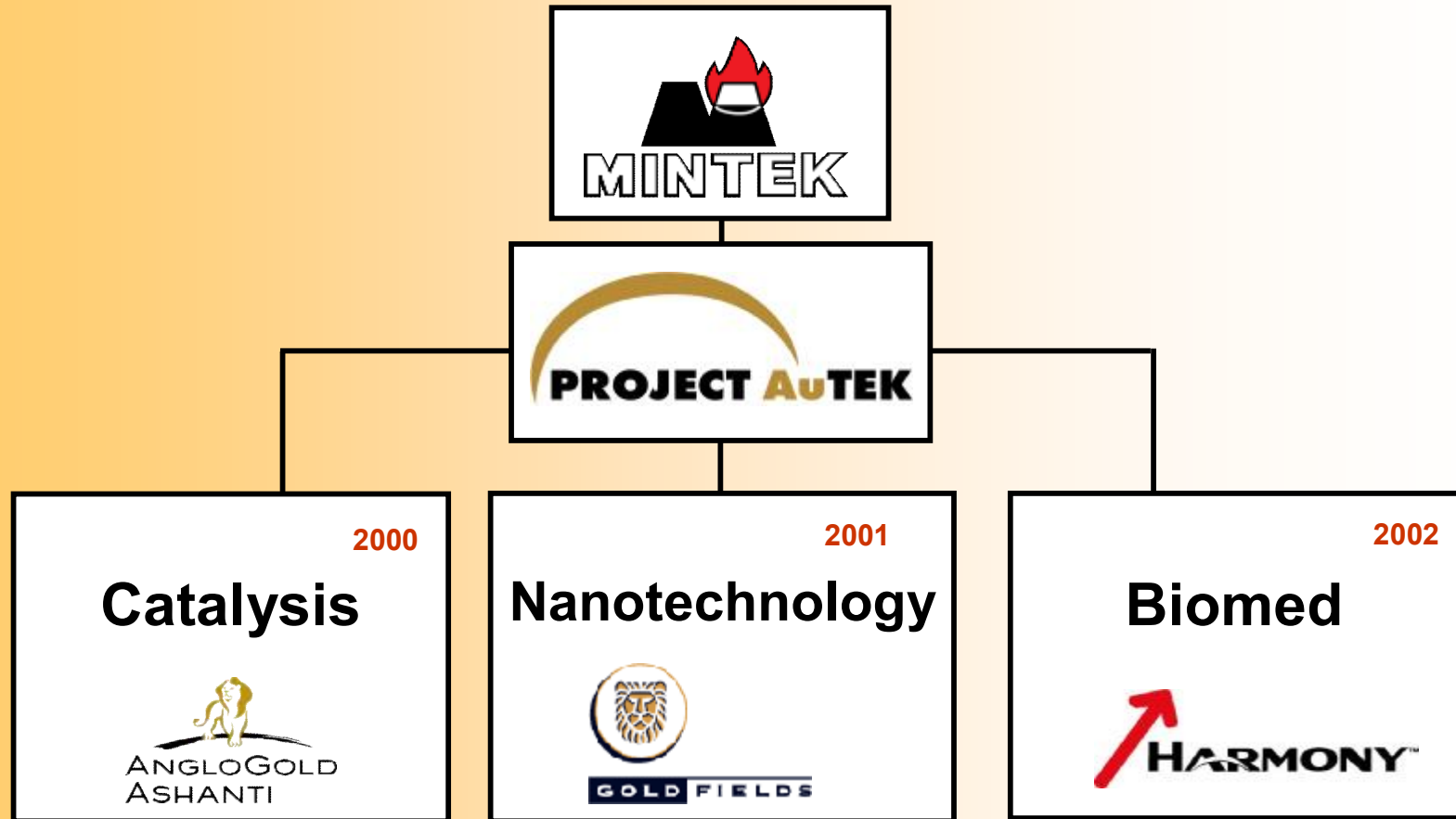
## AuTEK Biomed: The Biomedical Applications of Gold

**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

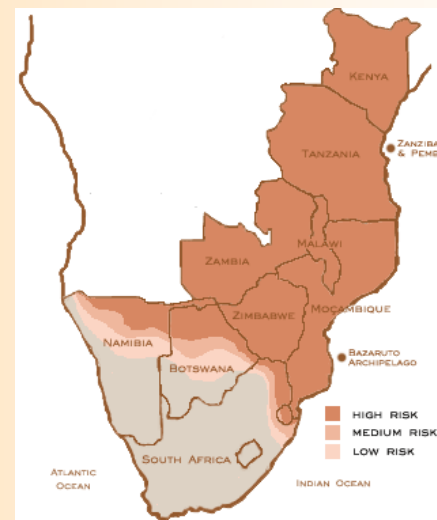
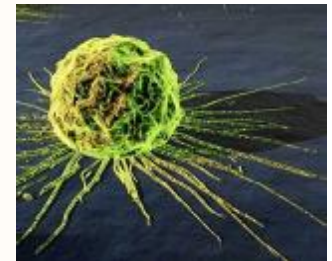
## Cancer in South Africa

An estimated 1 in 4 persons will develop cancer

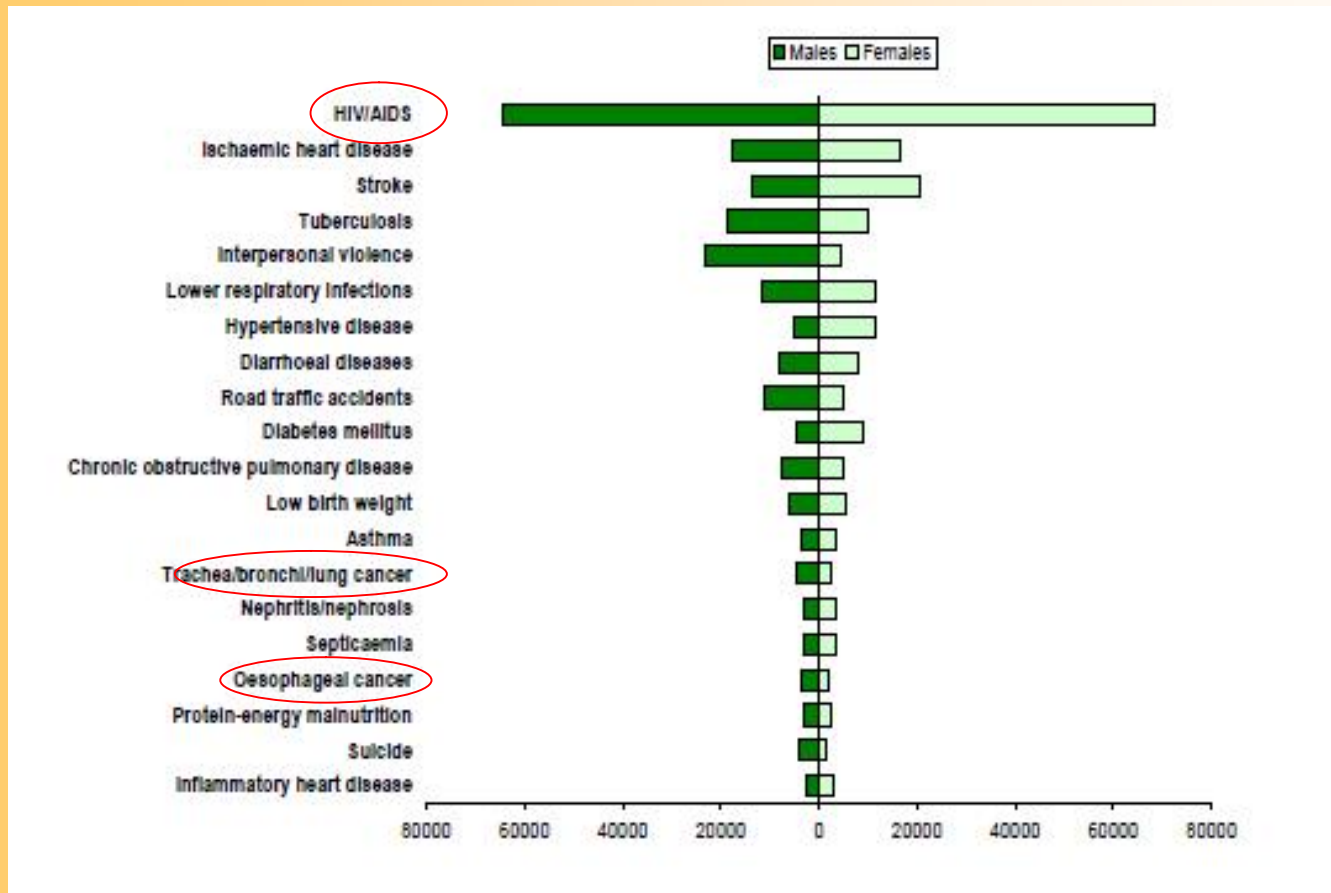
## Malaria in South Africa

+/- 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

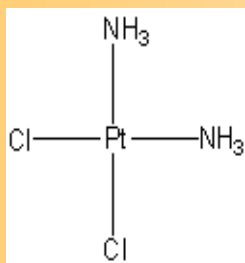
## Metals in Medicine

- 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 20<sup>th</sup> 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

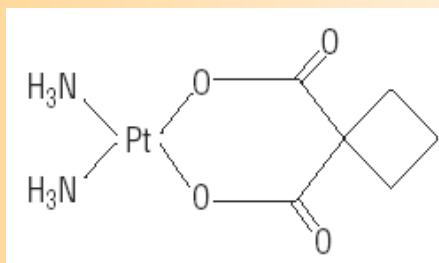


## Metals in Medicine

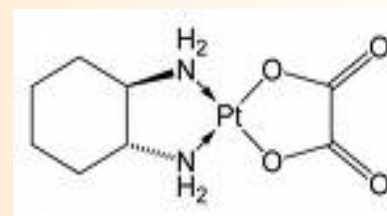
- Magnesium, aluminium oxides, calcium carbonate, bismuth subsalicylate – over the counter
- Lithium carbonate and sodium nitroprusside
- Serendipitous discovery of platinum drug, cisplatin
- Launched the search for improved platinum-based therapies and alternative metals for new therapeutic uses



Cisplatin



Carboplatin



Oxaliplatin

# AuTEK BIOMED

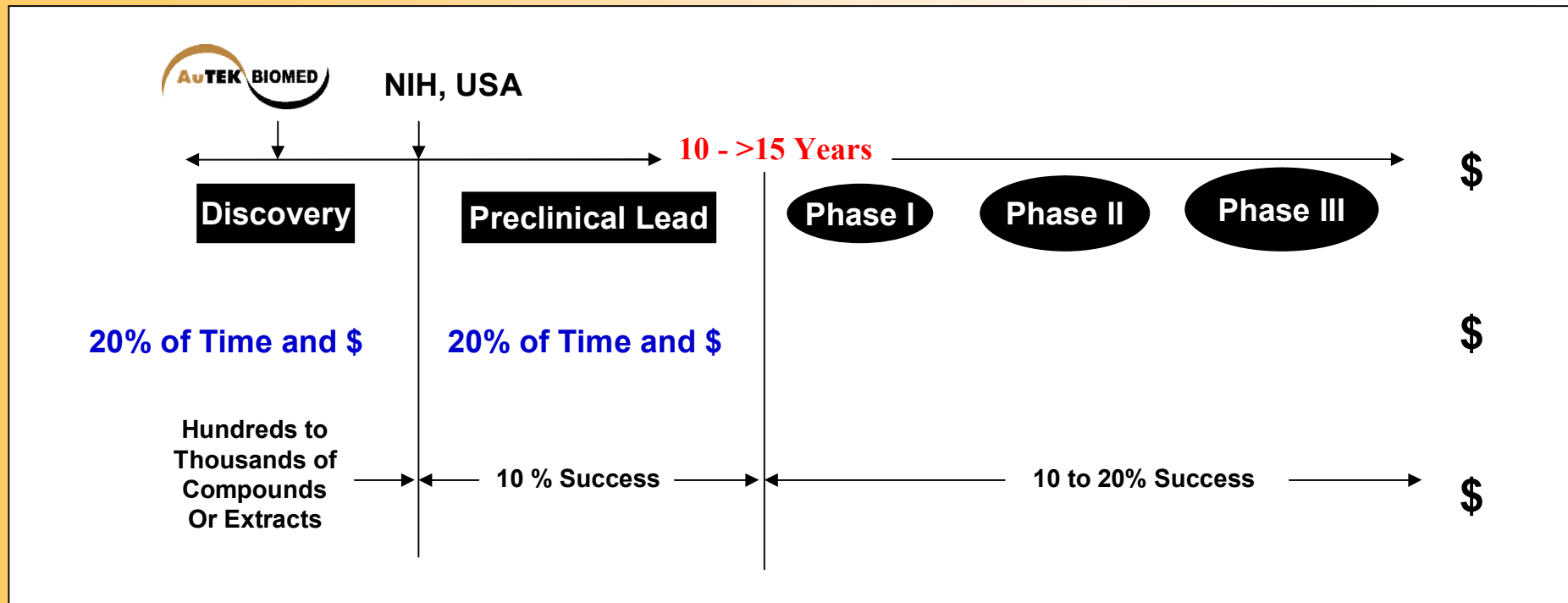
**AuTEK Biomed:** Early stage drug discovery in the field of:

**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

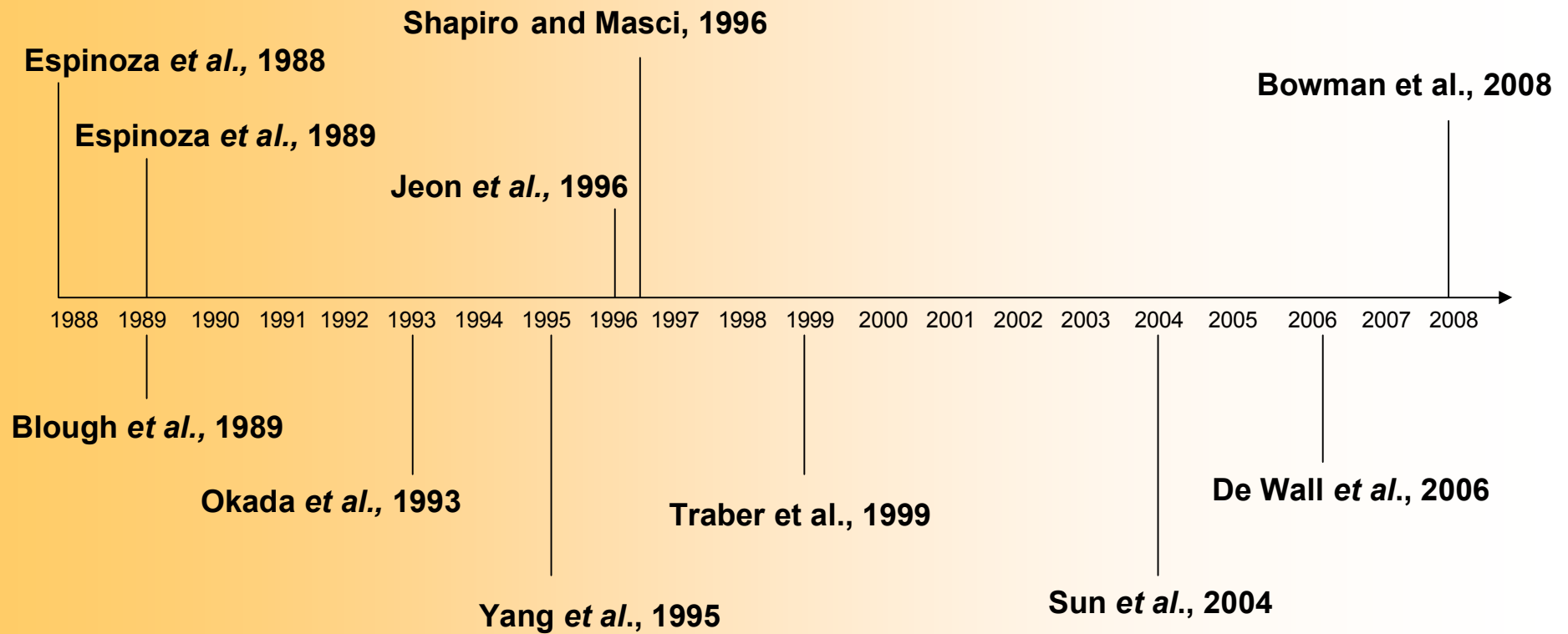
NIH, USA

COST, EU

## Industrial Partner



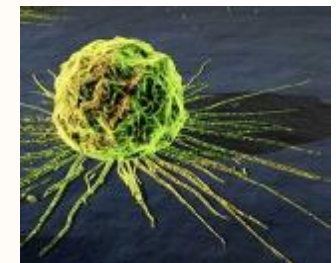
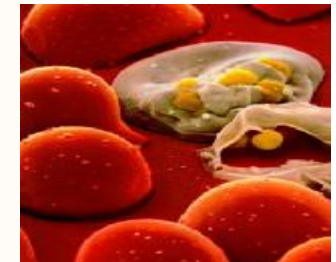
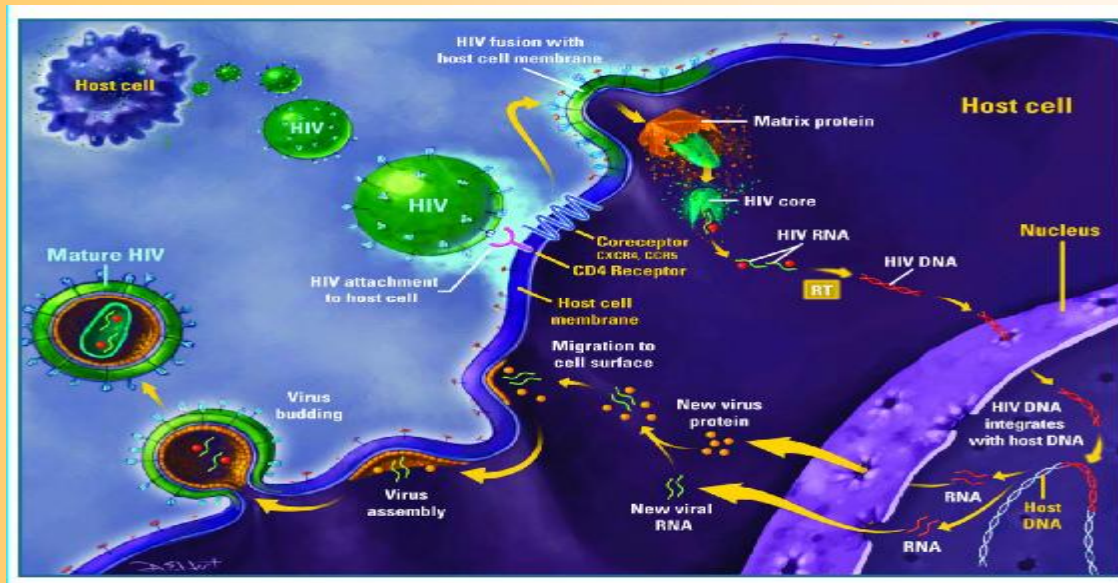
## Identifying gold-based anti-HIV agents



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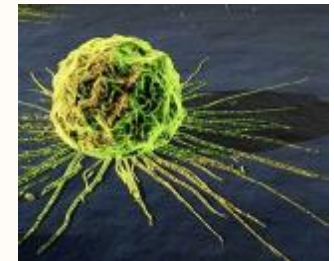
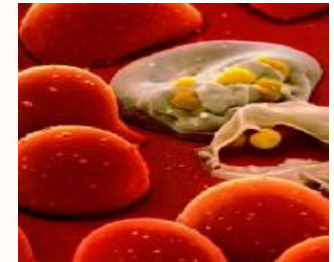
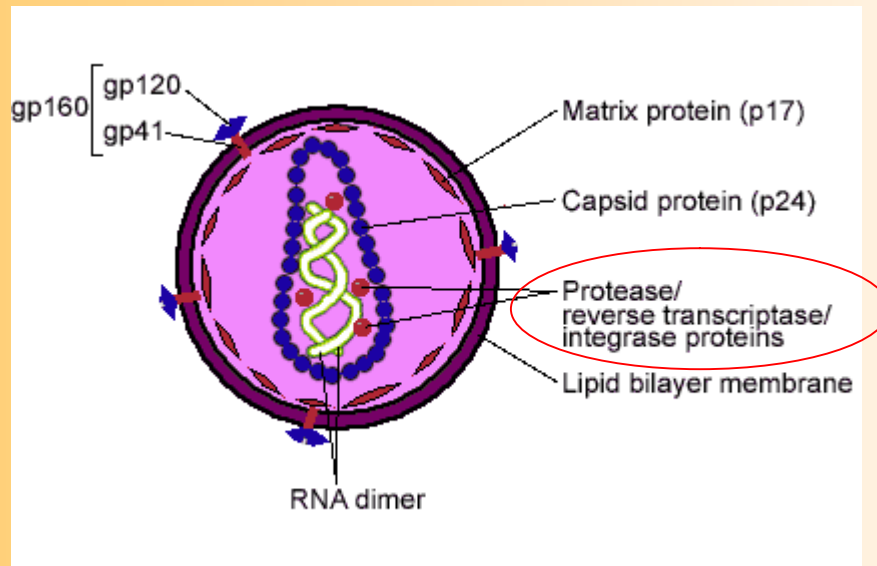
### 1. Rational design of gold compounds

- Target vital factors in the HIV lifecycle



## Identifying gold-based anti-HIV agents

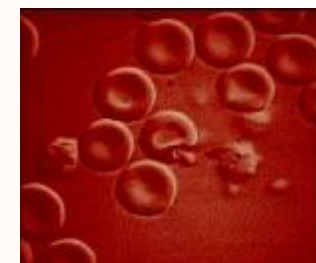
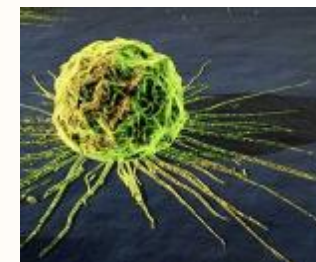
1. Rational design of gold compounds
  - Target vital factors in the HIV lifecycle



## Identifying gold-based anti-HIV agents

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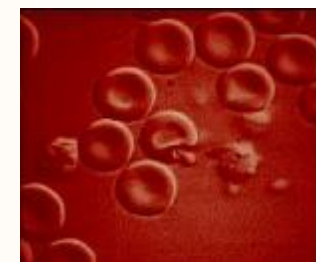
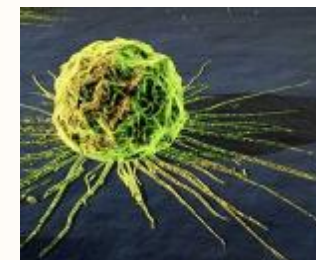
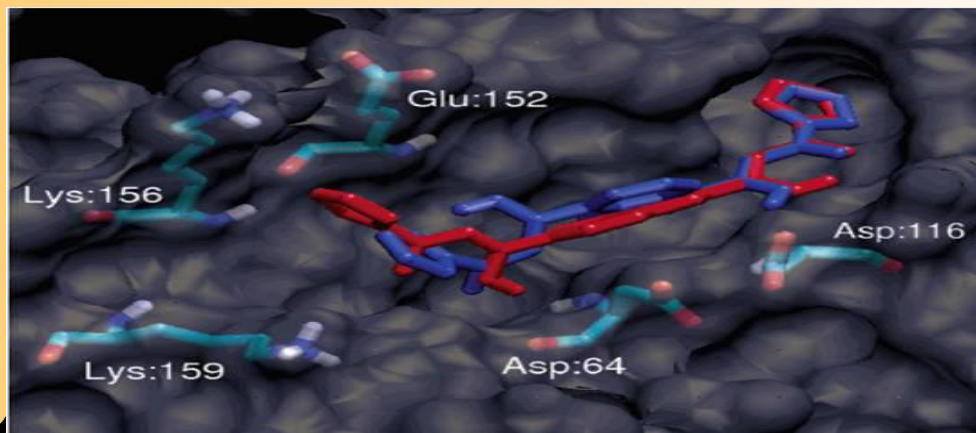
- Target vital factors in the HIV lifecycle
  - reverse transcriptase
  - protease
  - integrase
- Molecular models of HIV enzymes



## Identifying gold-based anti-HIV agents

### 1. Rational design of gold compounds

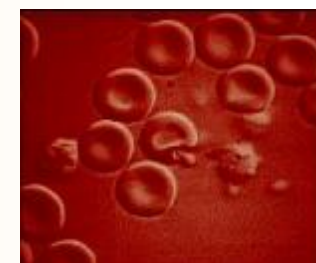
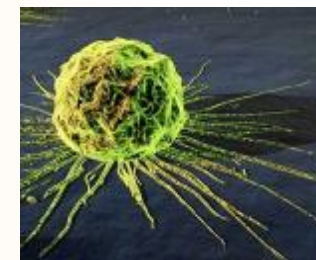
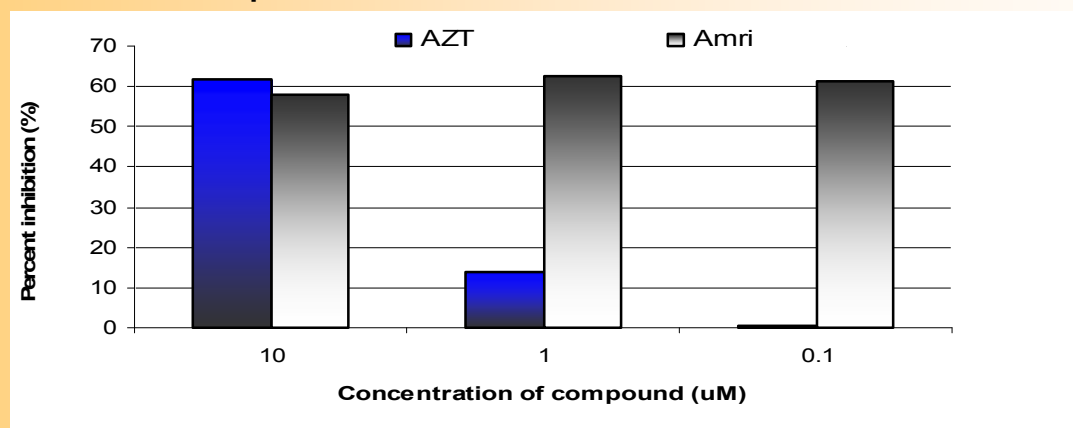
- Target vital factors in the HIV lifecycle
  - reverse transcriptase
  - protease
  - integrase
- Molecular models of HIV enzymes
- Focus on the active site



## Identifying gold-based anti-HIV agents

### 1. Rational design of gold compounds

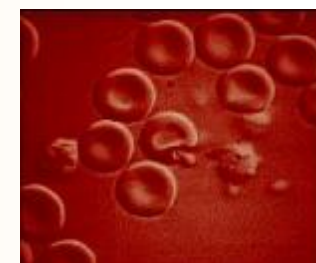
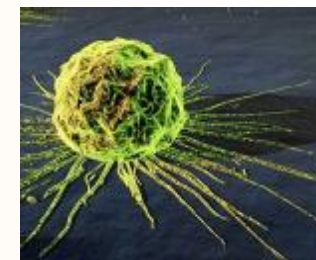
- Design compounds with high binding affinity to active site
- Synthesise a family of related compounds
- Evaluate these compounds in biological assays
- Results as to date:
  - Identified 59 compounds with high docking scores
  - 1 HIT compound



## Identifying gold-based anti-HIV agents

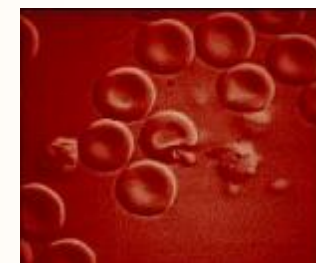
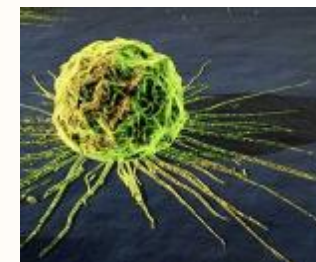
### 2. The traditional “Shotgun” approach

- 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



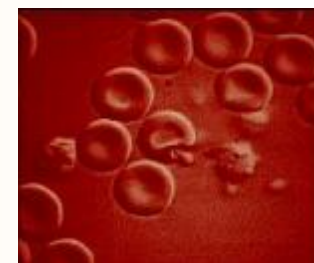
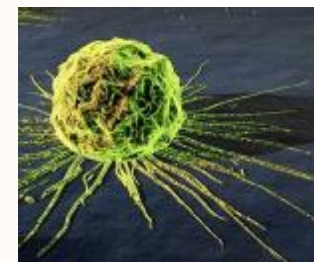
## Identifying gold-based anti-cancer and anti-malarial agents

- 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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