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OMICS Group International is an amalgamation of Open Access publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 400 online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 300 International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

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OMICS Group International is a pioneer and leading science event organizer, which publishes around 400 open access journals and conducts over 300 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

Development of aptamer based HIV-1 entry inhibitor prophylactic drugs

Grace London
CSIR, Biosciences
Emerging Health Technologies Platform
Pretoria, South Africa

2nd International Conference and Exhibition on Pathology

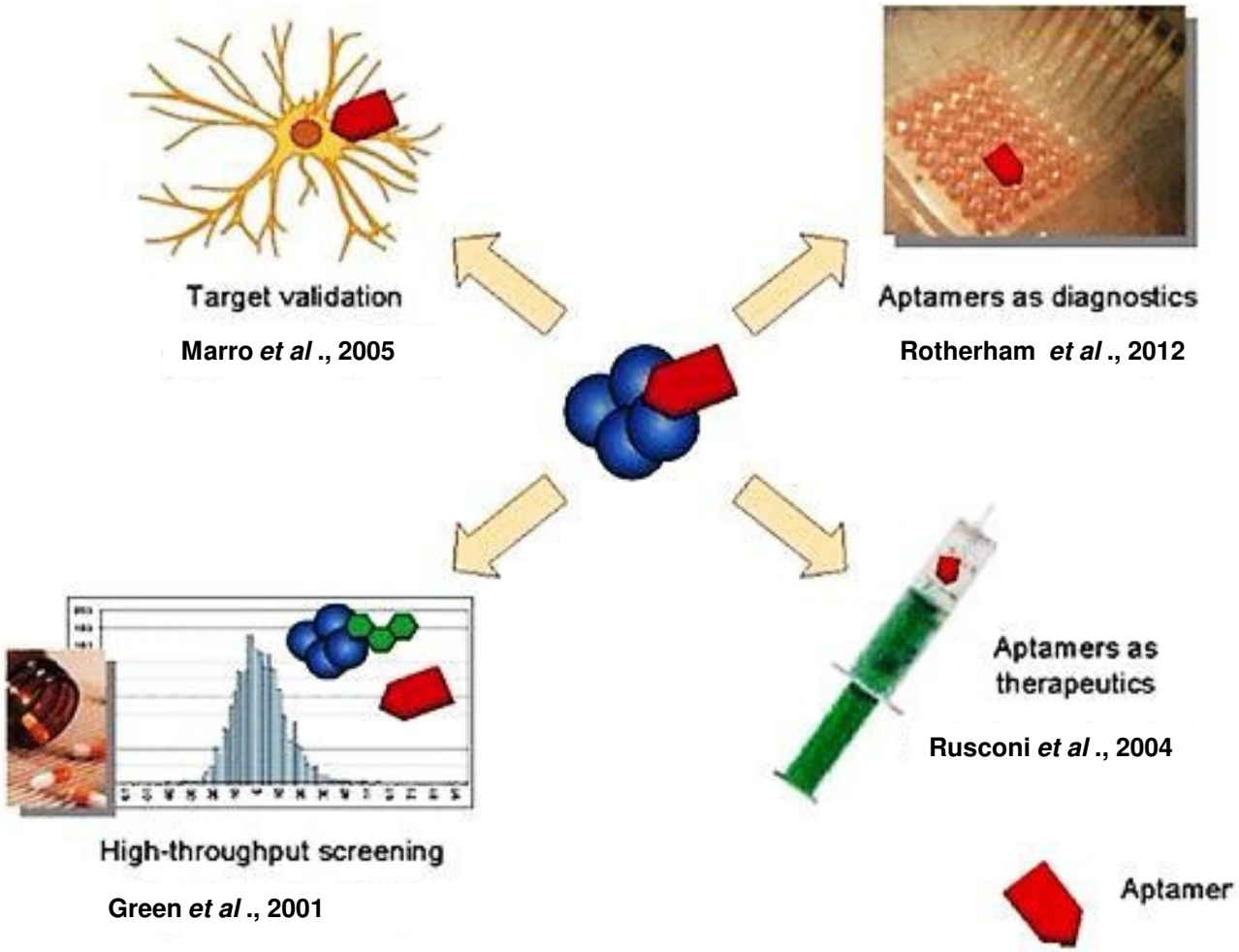
CSIR
our future through science

Properties of Aptamers

Joubert et al ., 2010

- Aptamers are nucleic acids with properties of antibodies
- Generated by simple in vitro process called SELEX
- High affinity and specificity
- Small in size and fold in 3 –D structure (e.g RNA aptamers)
- Resistant to nucleases and chemically stable
- Low toxicity and non-immunogenic

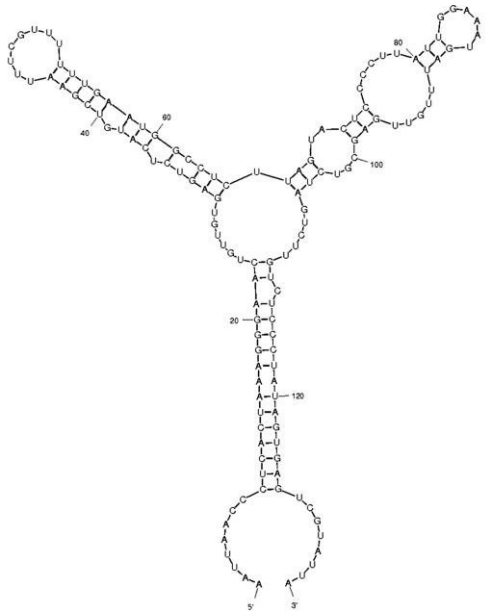
Applications of aptamers



Appl. Microbiol. Biotechnol., 2005, Nov 11, 1-8

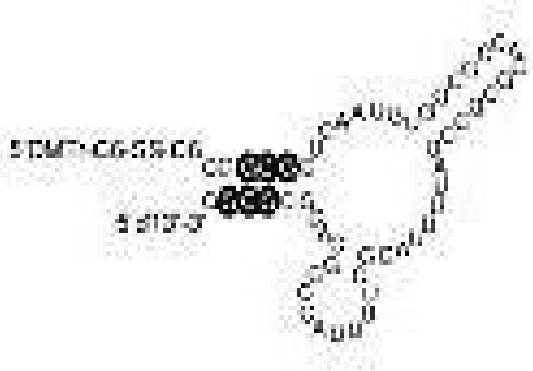
Anti-gp120 aptamers as HIV-1 entry inhibitors

Apt 1



Apt 1 bind gp120 trimer

Apt 2

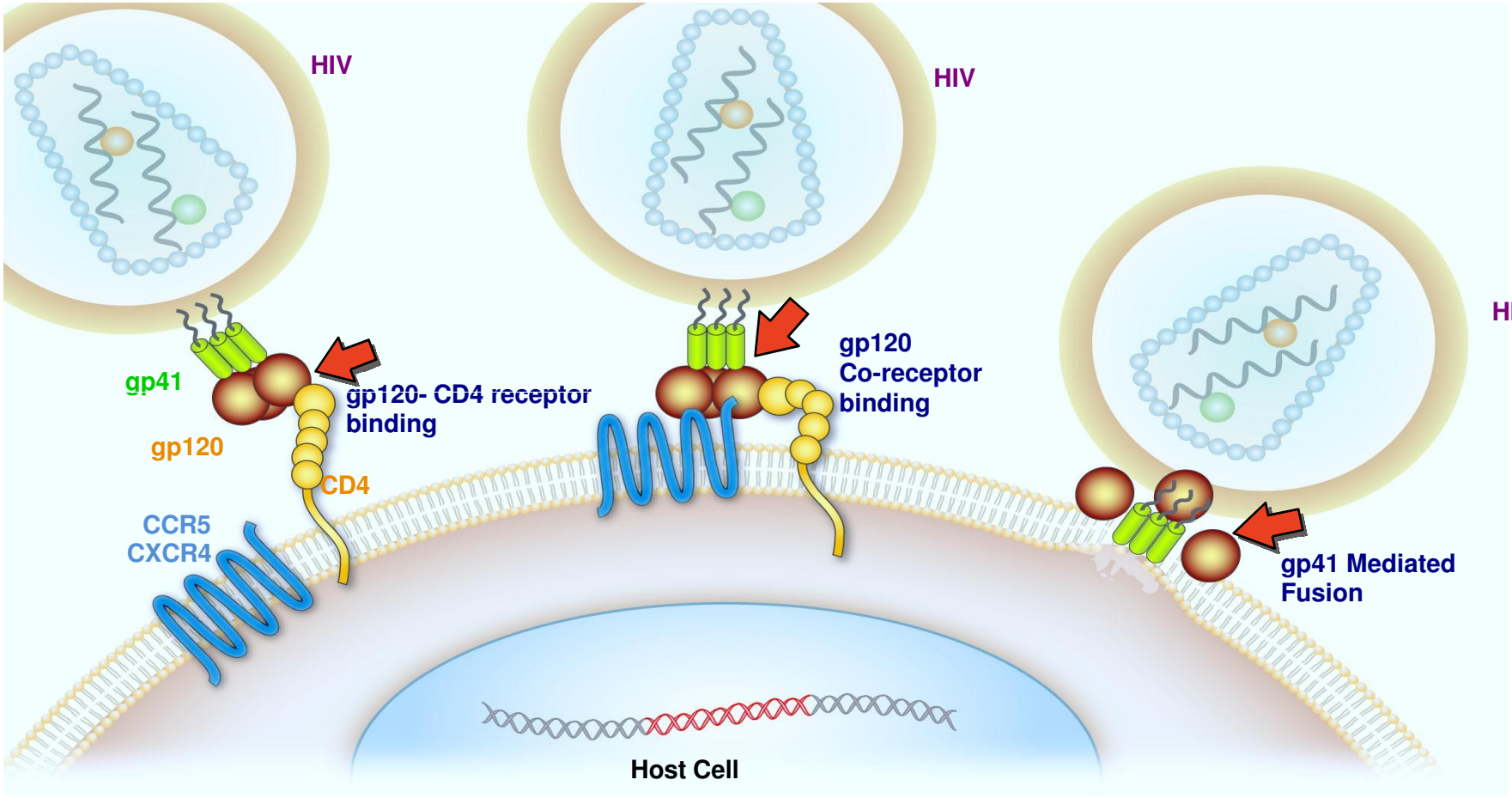


Apt 2 bind recombinant gp120

Apt = aptamer

Khati et al ., 2003; Cohen et al., 2008

HIV-1 entry and inhibitors



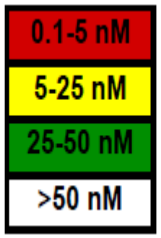
Pierson and Doms ., Current Top Microbiol Immunol (2003) 281 pp 1-27

Outline of the study

1. Evaluate efficacy of anti-gp120 aptamer against HIV-1 subtype C
2. Test toxicity
3. Map “aptatope’s ” on HIV-1 gp120
4. Test synergy with other entry inhibitors

Aptamers inhibit entry of HIV-1 subtype C Env pseudoviruses

			Aptamer IC_{50}	
Env clone	Stages of disease	Geographic location	Apt 1	Apt 2
CAP45.2.00.G3	Acute/early	S.Africa	2.6	0.3
ZM233M.PB6	Acute/early	Zambia	4.9	0.1
ZM249M.PL1	Acute/early	Zambia	>50	0.6
ZM53M.PB12	Acute/early	Zambia	20.1	0.8
ZM109F.PB4	Acute/early	Zambia	14.1	>50
ZM197M.PB7	Acute/early	Zambia	19.2	0.4
CAP210.200.E8	Acute/early	S.Africa	2.2	0.1
ZM135M.PL10a	Acute/early	Zambia	2.8	NT
ZM214M.PL5	Acute/early	Zambia	17.6	0.2
DU172.17	Acute/early	S.Africa	12.1	0.6
DU156.12	Acute/early	S.Africa	3.3	0.6
DU422.1	Acute/early	S.Africa	>50	0.3
CAP08.2.00.F6	Acute/early	S.Africa	1.2	1
CAP61.2.00.F10	Acute/early	S.Africa	0.3	0.4
CAP63.2.00.A9J	Acute/early	S.Africa	1.7	0.1
CAP84.2.00.32J	Acute/early	S.Africa	29.1	>50
CAP85.2.00.09J	Acute/early	S.Africa	16.1	0.1
CAP239.2.00.G3J	Acute/early	S.Africa	7.1	0.2
RP1.12*	Acute/early	S.Africa	4.7	0.6
RP4.3	Acute/early	S.Africa	>50	0.5
COT6.15	Chronic	S.Africa	0.9	>50
COT9.6	Chronic	S.Africa	6.1	>50
DU151.2	Acute/early	S.Africa	>50	>50
DU123.6	Acute/early	S.Africa	>50	>50
Conc	Acute/early	S.Africa	5	0.1
CAP288.2.00.5	Acute/early	S.Africa	9.5	0.3
CAP206.2.00.E8	Acute/early	S.Africa	3.8	0.7
CAP244.2.00.D3	Acute/early	S.Africa	2.3	0.4
RP6.6	Acute/early	S.Africa	3.7	0.4
CAP88.2.00.B6J	Acute/early	S.Africa	1.6	1
IN8362.25	Acute/early	India	18.2	NT
IN0013095.211	Acute/early	India	0.2	NT
% viruses neutralized			84%	79%
Mean IC_{50} (nM)			6.6 ± 8.1	0.4 ± 0.3



- 50 nM = No inhibition
- NT = Not titred
- * viruses using CXCR4 coreceptor

- Apt 1 = inhibited 84 % viruses
  - Mean IC_{50} 6.6 ± 8.1 nM
- Apt 2 = inhibited 79 % viruses
  - Mean IC_{50} 0.4 ± 0.3 nM

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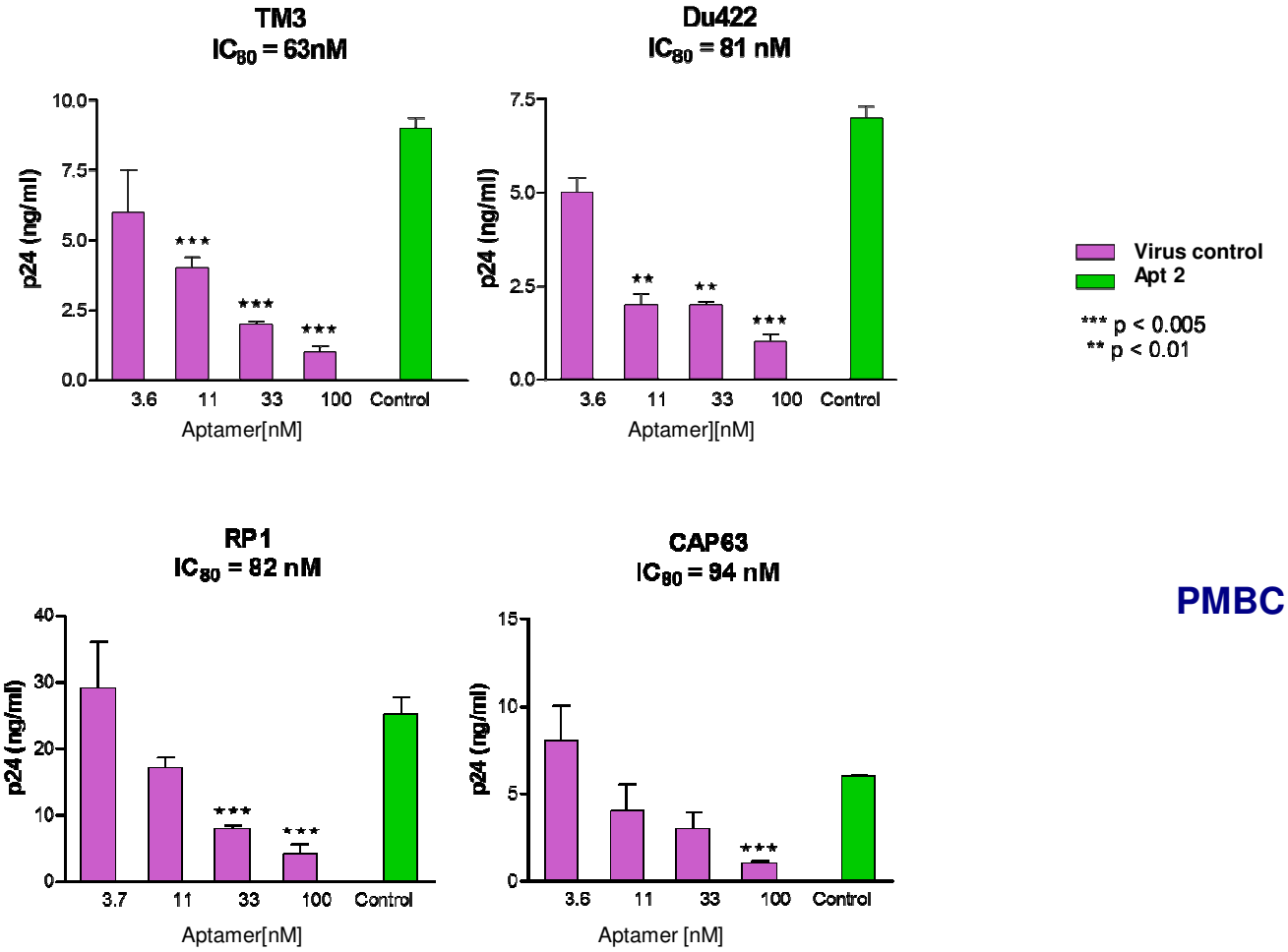
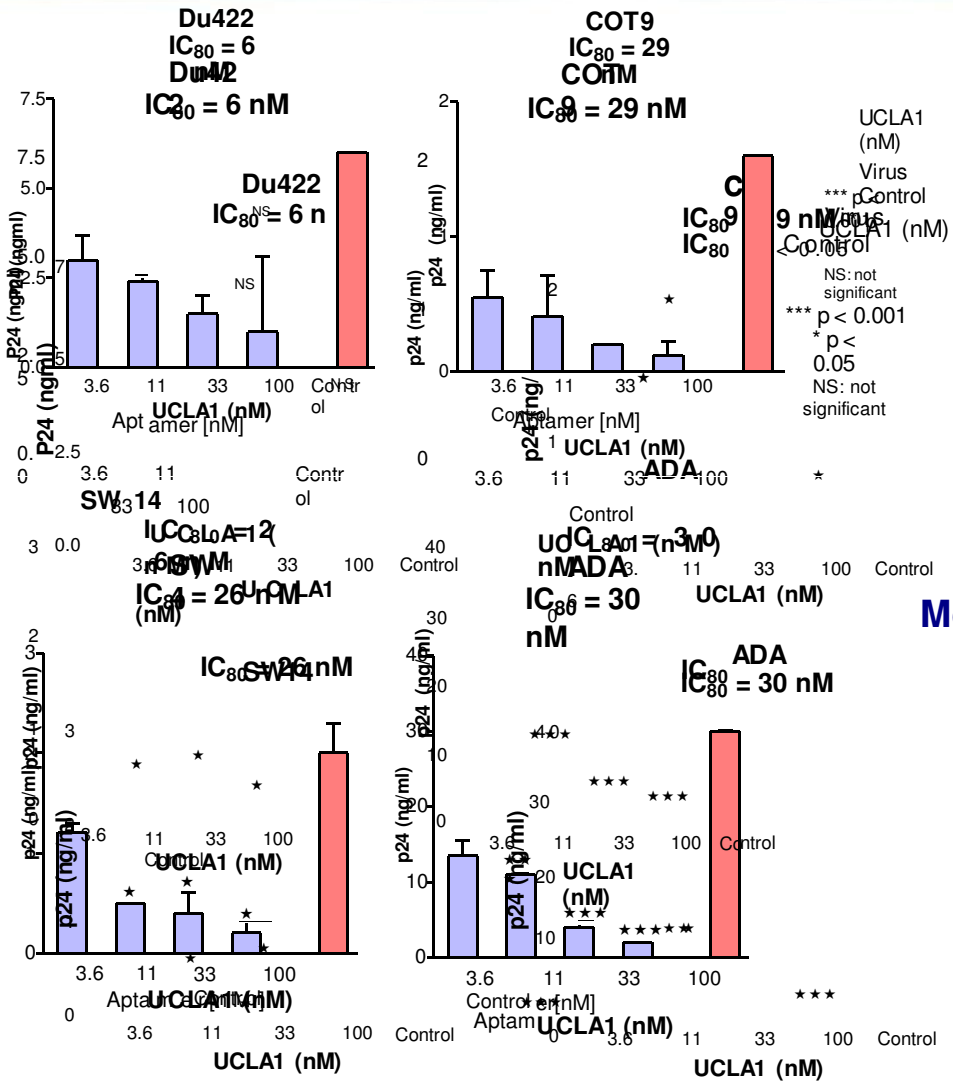
Aptamers inhibit entry of HIV-1 subtype C PBMC



PMBC = 80 ± 11.8 nM

Mufhandu, H *et al.*, J. Virol. (2012,)86(9), pp. 4989

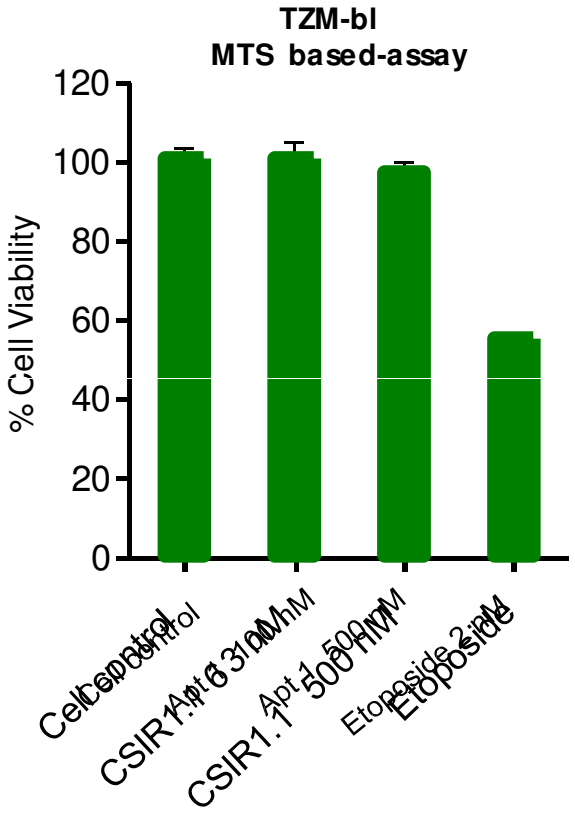
Aptamers inhibit entry of HIV-1 subtype C in Macrophages

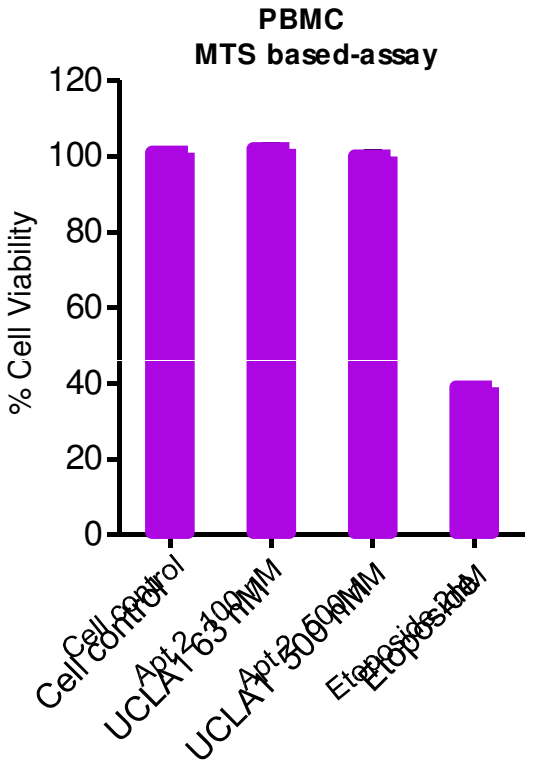


Mean IC_{80} in MDM = 23 ± 10.4 nM

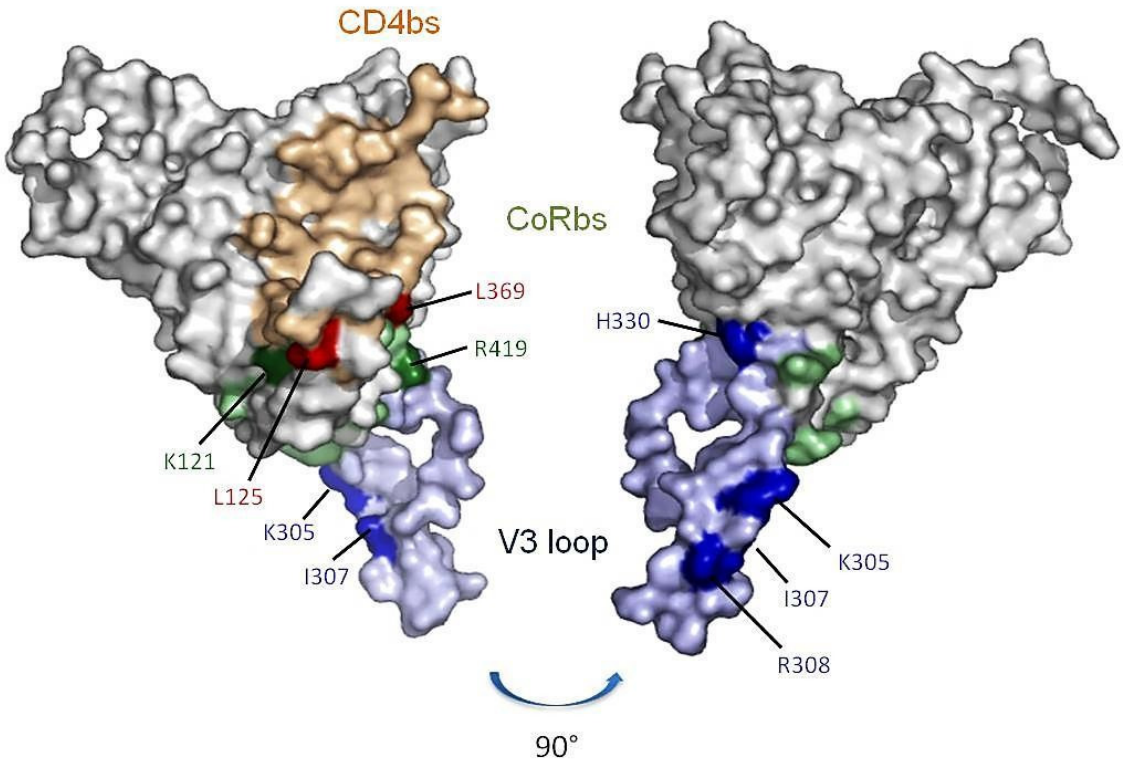
Mufhandu, H *et al.*, J. Virol. (2012,)86(9), pp. 4989

Aptamers exhibit no cytotoxicity





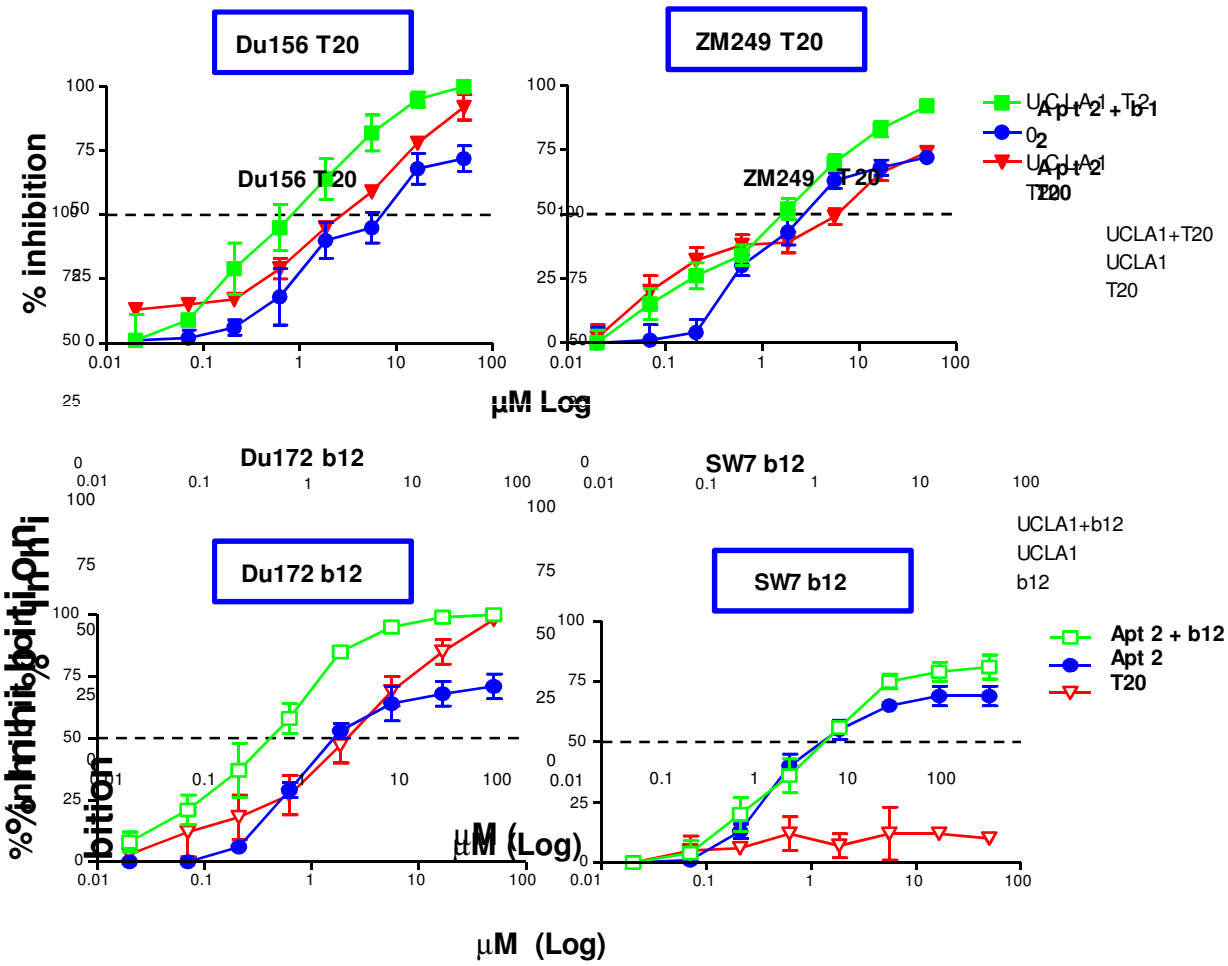
Aptamers interact with conserved residues on gp120



Aptamers bind to amino acids within the coreceptor (CoRbs) CCR5 binding site

Mufhandu, H *et al*., J. Virol. (2012,)86(9), pp. 4989

Synergy of aptamers with HIV-1 entry inhibitors



Synergism : CI = 0.3 – 0.9

Antagonism : CI = >1

Summary

- **Anti-gp120 RNA aptamer are efficacious against HIV-1 subtype C isolates (concentration in nanomolar)**
- They interact with conserved residues on gp120, delay virus resistance
- Not toxic in different cell types
- Synergy with other entry inhibitors, combination therapy with other drugs
- Anti-gp120 aptamers can be developed as entry inhibitor drugs

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