



Binding of eEF1A with the 5'UTR of HIV-1 genomic RNA is important for reverse transcription

Ting Wei PhD

Molecular Virology Laboratory
QIMR Berghofer Medical Research Institute



eEF1A review

Microbiology and Molecular Biology Reviews

The Unexpected Roles of Eukaryotic Translation Elongation Factors in RNA Virus Replication and Pathogenesis

Dongsheng Li, Ting Wei, Catherine M. Abbott and David Harrich

Microbiol. Mol. Biol. Rev. 2013, 77(2): 253



Aims

Investigated whether eEF1A can affect HIV-1 replication via binding with HIV-1 genomic RNA



Eukaryotic elongation factor 1 complex subunits are critical HIV-1 reverse transcription cofactors

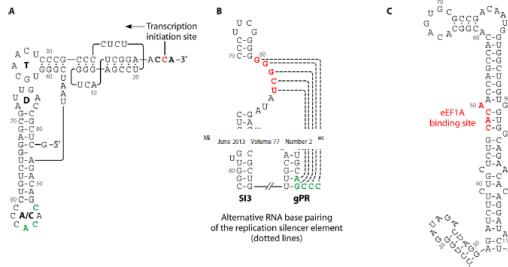
Kylie Warren^{a,b,1}, Ting Wei^{a,1}, Dongsheng Li^a, Fanyun Qin^a, David Warrilow^d, Min-Hsuan Lin^{b,2}, Haran Sivakumaran^c, Anna Agius^a, Catherine M. Abbott^d, Alun Jones^a, Jennifer A. Anderson^{a,b}, and David Harrich^{a,2}

^aDepartment of Cell and Molecular Biology, Queensland Institute of Medical Research, Herston, Queensland, 4022, Australia; ^bSchool of Natural Sciences, University of Western Sydney, Hawkesbury, New South Wales, 2751, Australia; ^cGuangxi Animal Centers for Disease Control, Nanning, Guangxi 530001, People's Republic of China; ^dPublic Health Virology Laboratory, Queensland Health Forensic and Scientific Services, Archerfield, Queensland, 4108, Australia; ¹Present address: Department of Biochemistry and Molecular Biology, University of Queensland, St. Lucia, Queensland, 4072, Australia; ²Queensland Molecular Medicine Centre, Institute of Genetics and Molecular Medicine, Western General Hospital, University of Edinburgh, Edinburgh EH4 2XU, United Kingdom; Institute for Molecular Bioscience, University of Queensland, St. Lucia, Brisbane, Queensland, 4072, Australia; ³Centre for Virology, Burnet Institute, Melbourne, Victoria, 3004, Australia; and ⁴Department of Medicine, Monash University, Melbourne, Victoria, 3004, Australia

PNAS | June 12, 2012 | vol. 109 | no. 24 | 9587–9592



eEF1A review

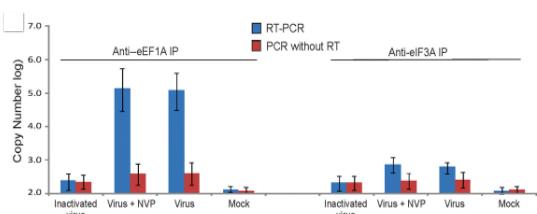


Li et al. Microbiology and Molecular Biology Reviews, June 2013 Vol 77



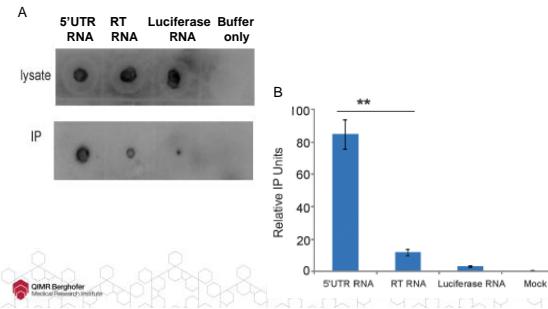
eEF1A binds to HIV-1 genomic RNA

Reversible crosslink co-immunoprecipitation (RC-co-IP)



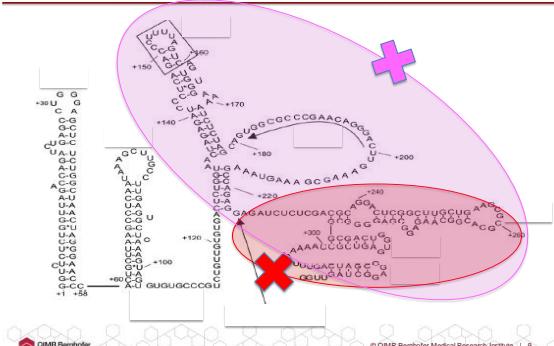
eEF1A binds directly to 5' UTR of HIV-1 RNA

RNA transfection + RC-co-IP



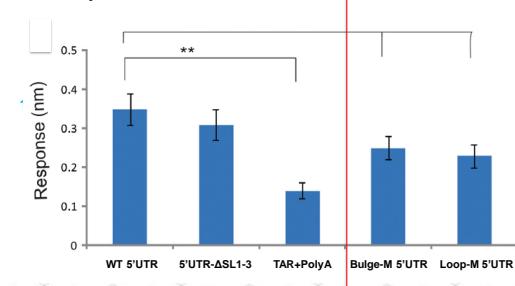
© QMIR Bergfelder Medical Research Institute

Predicted secondary structure of 5' UTR



Important site for eEF1A binding

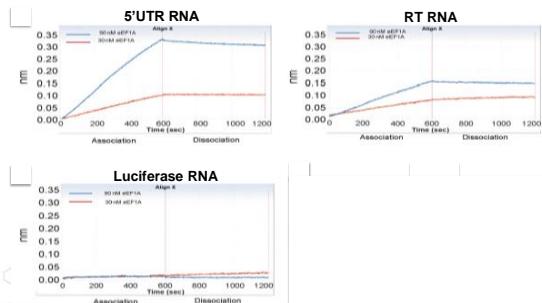
Stem-loop with TLE



© QMIR Bergfelder Medical Research Institute

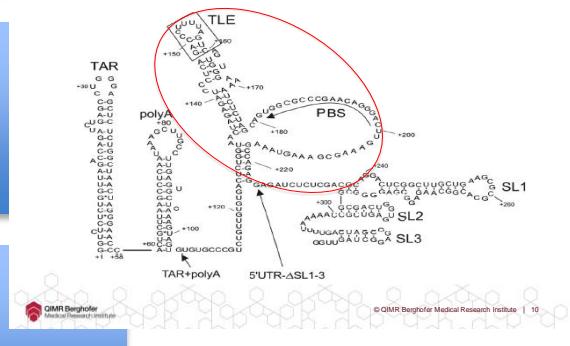
eEF1A binds to 5' UTR of HIV-1 RNA

Biolayer Interferometry (BLI) assay

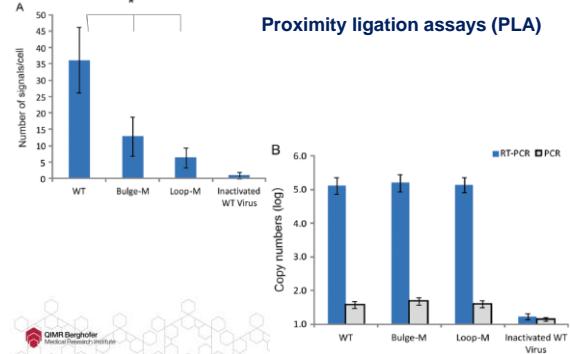


Important site for eEF1A binding

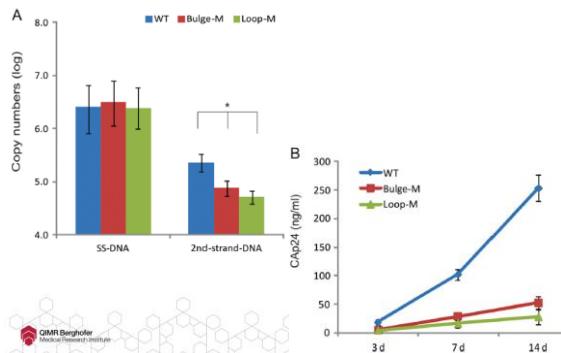
106-224 of 5'UTR



5'UTR mutations reduce eEF1A-RT association



5'UTR mutations affect HIV-1 RTn

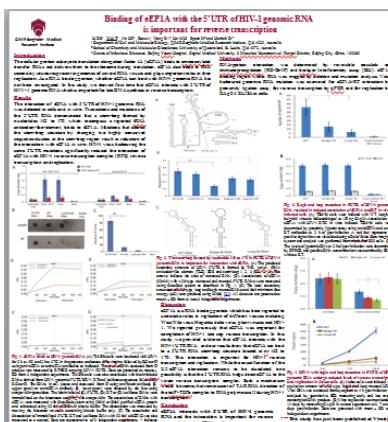


© QIMR Berghofer Medical Research Institute | 13

Conclusion

eEF1A interacts with 5'UTR of HIV-1 genomic RNA so that affect reverse transcription efficiency

© QIMR Berghofer Medical Research Institute | 14



Poster

Theme A

No.10

© QIMR Berghofer Medical Research Institute | 17

Summary

- ❖ eEF1A binds directly to 5' UTR of HIV-1 genomic RNA
- ❖ 142-170 stem-loop at 5'UTR RNA is important for eEF1A-RT binding
- ❖ Stem-loop mutations affect HIV-1 reverse transcription and replication

© QIMR Berghofer Medical Research Institute | 14

Paper just published

Open Access Highly accessed

Urat et al. Virology Journal (2015) 12:188
DOI 10.1186/s12931-015-0337-x

VIROLOGY JOURNAL

RESEARCH

Open Access

Binding of the eukaryotic translation elongation factor 1A with the 5'UTR of HIV-1 genomic RNA is important for reverse transcription

Dongsheng ¹*, Ting Wei ¹, Hongping Jin ¹, Amanda Rose ², Rui Wang ³, Min-Hsuan Lin ², Kirsten Spann ²
and David Harrich ¹*

© QIMR Berghofer Medical Research Institute | 16

Acknowledgements



QIMR Berghofer
Medical Research Institute

Molecular Virology Laboratory

David Harrich
Dongsheng Li
Hongping Jin
Amanda Rose
Rui Wang
Min-Hsuan Lin
Lina Rustanti
Kirsten Spann
Jennifer Cao
Daniel Rawle
Sarah Wang



National Health and Medical Research Council

© QIMR Berghofer Medical Research Institute | 18