Vladimir A. Kuznetsov
Bioinformatics Institute
Singapore

Introduction to R-loop biology.

R-loops, which are three-stranded RNA and DNA hybrid structures, can be crucial to many normal biological processes and have also been associated with triggering mutations, DNA breaks and diseases. These hybrid structures provide intriguing possibilities for use as novel targets for diagnostics and treatment of diseases including cancer, autoimmune and neurodegenerative conditions. Here we review the current knowledge of the mechanisms and computational models of R loops, controlling mechanisms of R-loop formation and their putative relationship with diseases.

R-петли - гибридные структуры, образованные тремя нитями РНК и ДНК, которые могут иметь ключевое значение во многих нормальных биологических процессах, а также ассоциируются с появлением мутаций, разрывами ДНК и возникновением ряда патологий. Эти гибридные структуры обеспечивают впечатляющие возможности в качестве новых мишеней для диагностики и лечения рака, аутоиммунных и нейродегенеративных заболеваний. Мы рассмотрим текущее знание механизмов возникновения и компьютерные модели R петлей, механизмы контроля формирования R-петлей, и их предполагаемые взаимосвязи с патологическими процессами.

Specific topics: We discuss also how RNA processing defects could destabilize genomes through mutagenic R-loop structures and by altering expression of genes required for genome stability and functional activity genetic disease-related pathways. We propose an analytical model and computational tool to rapidly and accurately predict (>90%) the locations of R-loop Forming Sequences (RLFSs) in any genome or artificial nucleic acid sequences. The high prediction accuracy would significantly accelerate R-loop detection and dramatically reduce the cost and time taken compared to currently available experimental methods, paving the way for further improvement and development in the nascent but rapidly developing field of R-loop biology.

Selected Publications 2015:

1: Aswad L, Yenamandra SP, Ow GS, Grinchuk O, Ivshina AV, Kuznetsov VA#. Genome and transcriptome delineation of two major oncogenic pathways governing invasive ductal breast cancer development. Oncotarget. 2015 Oct 10. doi:10.18632/oncotarget.5543. PubMed PMID: 26474389. **2**: Jenjaroenpun P, Chew CS, Yong TP, Choowongkomon K, Thammasorn W, Kuznetsov VA.# The TTSMI database: a catalog of triplex target DNA sites associated with genes and regulatory elements in the human genome. Nucleic Acids Res. 2015; Jan; 43(Database issue):D110-6. doi: 10.1093/nar/gku970. PubMed PMID: 25324314; PubMed Central PMCID: PMC4384029. **3**: Jenjaroenpun P, Wongsurawat T, Yenamandra SP, Kuznetsov VA# . QmRLFS-finder: a model, web server and stand-alone tool for prediction and analysis of R-loop forming sequences. Nucleic Acids Res. 2015 Apr 16. pii: gkv344. [Epub ahead of print] PubMed PMID: 25883153. **4**: Lim KW, Jenjaroenpun P, Low ZJ, Khong ZJ, Ng YS, Kuznetsov VA#, Phan AT#. Duplex stem-loop-containing quadruplex motifs in the human genome: a combined genomic and structural study. Nucleic Acids Res. 2015 May 9. pii: gkv355. PubMed PMID: 25958397. **5**: Grinchuk O, Efthymios Motakis, Yenamandra SP, Ow GS, Jenjaroenpun P, Tang Zhiqun, A. Yarmishyn1, Ivshina AV, Kuznetsov VA#. Sense-antisense gene-pairs in breast cancer and associated pathological pathways. Oncotarget 2015.Oct 25; DOI: 10.18632/oncotarget.6255. **6:** Giannakakis A, Zhang J, Jenjaroenpun P, Nama S, Zainolabidin N, Aau MY, Yarmishyn AA, Vaz C, Ivshina AV, Grinchuk OV, Voorhoeve M, Vardy LA, Sampath P, Kuznetsov VA#, Kurochkin IV#, Guccione E#. Contrasting expression patterns of coding and noncoding parts of the human genome upon oxidative stress. Sci Reports. 2015 May 29;5:9737. doi: 10.1038/srep09737. PubMed PMID: 26024509. **7**: Ow GS and Kuznetsov VA.# Multiple signatures of a disease in potential biomarker space: Getting the signatures consensus and identification of novel biomarkers. BMC Genomics 2015, 16(Suppl 7):S2 doi:10.1186/1471-2164-16-S7-S2
8: Goh WQJ, Ow GS, Kuznetsov VA, Chong S, Lim YP. DLAT subunit of the pyruvate dehydrogenase complex is up-regulated in gastric cancer-implications in cancer therapy. American Journal of Translational Research. 2015;7(6):1140-1151. **9**:Nymoen DA, Hetland Falkenthal TE, Holth A, Ow GS, Ivshina AV, Tropé CG, Kuznetsov VA, Staff AC, Davidson B. Expression and clinical role of chemoresponse-associated genes in ovarian serous carcinoma. Gynecol Oncol. 2015 Jul 29. pii: S0090-8258(15)30091-3. doi:10.1016/j.ygyno.2015.07.107.
#: corresponding author