Title: Challenges in defining the role of intron retention in normal biology and disease

Authors: Darya P. Vanichkina, Ulf Schmitz, Justin J.-L. Wong, John E.J. Rasko

PII: S1084-9521(17)30293-8
DOI: http://dx.doi.org/doi:10.1016/j.semcdb.2017.07.030
Reference: YSCDB 2293

To appear in: *Seminars in Cell & Developmental Biology*

Received date: 12-6-2017
Revised date: 19-7-2017
Accepted date: 19-7-2017

Please cite this article as: Vanichkina Darya P, Schmitz Ulf, Wong Justin J-L, Rasko John E.J.Challenges in defining the role of intron retention in normal biology and disease.*Seminars in Cell and Developmental Biology* http://dx.doi.org/10.1016/j.semcdb.2017.07.030

Challenges in defining the role of intron retention in normal biology and disease

Darya P. Vanichkina[1,2], Ulf Schmitz[1,2], Justin J.-L. Wong[1,2,3], John E. J. Rasko[1,2,4]

[1] Gene & Stem Cell Therapy Program, Centenary Institute, University of Sydney, Camperdown 2050, Australia
[2] Sydney Medical School, University of Sydney, Camperdown 2050, Australia
[3] Gene Regulation in Cancer Laboratory, Centenary Institute, University of Sydney, Camperdown 2050, Australia
[4] Cell and Molecular Therapies, Royal Prince Alfred Hospital, Camperdown 2050, Australia

Corresponding author: John E.J. Rasko, j.rasko@centenary.org.au

Highlights

- Intron retention is a mechanism of gene expression control in eukaryotes
- Custom computational pipelines are essential for IR detection
- Phylogenetic analyses reveal conserved IR and functional consequences
- Subcellular fractionation helps determine the spatio-functional relationship of IR
- Improvements in mass spectrometry are critical to detect novel IR-derived peptides

Abstract

RNA sequencing has revealed a striking diversity in transcriptomic complexity, to which alternative splicing is a major contributor. Intron retention (IR) is a conserved form of alternative splicing that was originally overlooked in normal mammalian physiology and development, due mostly to difficulties in its detection. IR has recently been revealed as an independent mechanism of controlling and enhancing the complexity of gene expression. IR facilitates rapid responses to biological stimuli, is involved in disease pathogenesis, and can generate novel protein isoforms. Many challenges, however, remain in detecting and quantifying retained introns and in determining their effects on cellular phenotype. In this review, we provide an overview of these challenges, and highlight approaches that can be used to address them.

Keywords

- alternative splicing
- RNA sequencing
- Bioinformatics
- gene expression