RNA Biology 10:4, 463-464; April 2013; © 2013 Landes Bioscience

Landes Highlights

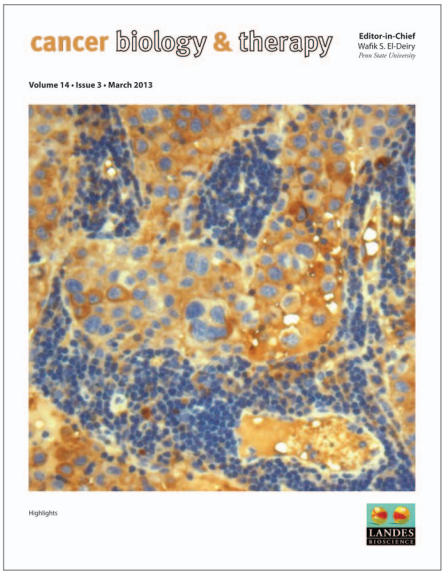
Role of microRNAs in breast cancer

Ramesh Singh and Yin-Yuan Mo

MicroRNAs (miRs) are a class of post-transcriptional gene regulators with critical functions in normal cellular as well as disease processes. Since their discovery in the early 1990s, a large number of miRs have been characterized and analyzed to understand their pivotal role and their impact in a myriad of biological processes. They were found to be involved in a variety of human diseases such as neurodegenerative disorders, diabetes, cardiac hypertrophy, respiratory diseases and cancer. The role of miRs in breast cancer is the subject of a recent review by Drs Ramesh Singh and Yin-Yuan Mo. Breast cancer is the best studied cancer in terms of pathobiology, subtypes and treatment, and the role of miRs in this cancer is well established. A plethora of miRs have been reported to be implicated in breast cancer initiation, progression and/or metastasis, and in the current review, the authors discuss three groups of miRs which can act as oncogene, tumor suppressor or play a role in breast cancer therapy resistance. A better understanding of the miR-guided network could open new windows for diagnostics and therapy of breast cancer.
www.landesbioscience.com/journals/cbt/article/23296

Reference

Singh R, et al. Cancer Biol Ther 2013; 14:201-12.



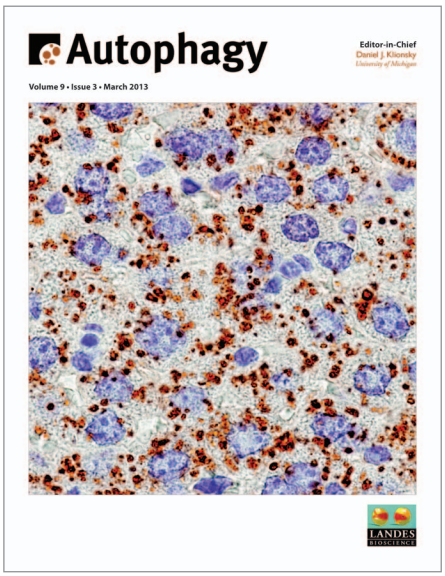
Novel type of autophagy discovered: RNAutophagy

Yuuki Fujiwara, Akiko Furuta, Hisae Kikuchi, Shu Aizawa, Yusuke Hatanaka, Chiho Konya, Kenko Uchida, Aya Yoshimura, Yoshitaka Tamai, Keiji Wada and Tomohiro Kabuta

Regulated degradation of cellular components by lysosomes is essential to maintain biological homeostasis. In mammals, three forms of autophagy have been identified: macroautophagy, microautophagy and chaperone-mediated autophagy (CMA). In a new study, Dr Tomohiro Kabuta and colleagues reported a novel type of autophagy, in which RNA is taken up directly into lysosomes for degradation. They termed the pathway "RNautophagy." RNautophagy is ATP-dependent, and unlike CMA, independent of heat shock 70 kDa protein 8 (HSPA8/Hsc70). Lysosome-associated membrane protein 2 C (LAMP2C) serves as a receptor for this pathway. The cytosolic tail of LAMP2C specifically binds to almost all total RNA derived from mouse brain. The cytosolic sequence of LAMP2C and its affinity for RNA are evolutionarily conserved from nematodes to humans. The study findings shed light on the mechanisms underlying RNA homeostasis in higher eukaryotes.
www.landesbioscience.com/journals/autophagy/article/23002

Reference

Fujiwara Y, et al. Autophagy 2013; 9:403-9.



Early dynamics of the human rRNA processing

Alexey Popov, Evgeny Smirnov, Lubomír Kováčk, Otakar Raška, Guy Hagen, Lenka Stixová and Ivan Raška

The RNA polymerase I generates the largest fraction of all newly synthesized RNAs in growing eukaryotic cells by producing a single large rRNA precursor. This primary transcript (47S in mammalian species) undergoes a series of cleavages, resulting in three rRNAs: 18S, 5.8S and 28S. The rRNA processing consists in removing so-called external transcribed spacers (5′ETS and 3′ETS) and internal transcribed spacers (ITS), of which eukaryotic cells have at least two. The spacer sequences vary greatly in composition and length in different organisms, though the core elements in the mature rRNAs are highly conserved. The sequence of the main processing events in human cells has been established, but little is yet known about the dynamics of this process, especially the dynamics of its early stages. In a recent study, Dr Ivan Raška and colleagues used real-time PCR to measure levels of pre-rRNA after inhibition of transcription with actinomycin D. Thus, they could estimate the half-life time of rRNA transcripts in two human-derived cell lines, as well as in mouse cells. The primary transcripts seemed to be more stable in the human than in the murine cells. Remarkably, the graphs in all cases showed more or less pronounced lag phase, which may reflect preparatory events preceding the first cleavage of the pre-rRNA. Additionally, the authors followed the dynamics of the decay of the 5′ETS fragment, which is degraded only after the formation of 41S rRNA. Based on the study results, the authors estimate that the corresponding three (or four) steps of the processing in human cells take five to eight minutes.

www.landesbioscience.com/journals/nucleus/article/23985

Reference

Popov A, et al. Nucleus 2013; 4:134-41.

News on the origin of spliceosomal introns

Jérôme Collemare, Ate van der Burgt and Pierre J.G.M. de Wit

Eukaryotic genes consist of exons that contain the coding sequence, and of introns that are non-coding and are removed from premature mRNA after transcription. The origin of spliceosomal introns is still unknown, and analyses of gain and loss of introns in diverse eukaryotic lineages kept the mystery on introns' origin alive because there was less evidence for gains as compared with losses. Several mechanisms have been proposed for intron gains, but the majority of these models only rely on indirect evidence and fail to describe how the vast majority of introns were gained. None of the models can explain the high numbers of introns present in numerous Eukaryotes. The recent discovery of introner-like elements (ILEs) in six fungal species shed new light on the origin of regular spliceosomal introns (RSIs) and the mechanism of intron gains. Dr Collemare and coworkers found these novel spliceosomal introns in hundreds of copies, which are longer than RSIs and harbor stable predicted secondary structures. Yet, they are prone to degeneration in sequence and length to become undistinguishable from RSIs, suggesting that ILEs are predecessors of most RSIs. In that study, the authors performed a simple BlastN search and clustering method to identify ILEs. Depending on the number of introns with a near-identical sequence and whether they were duplicated within the same gene or in different genes, these multi-copy introns were classified as same gene duplications (SGD), low-copy introns (LCI) and high-copy introns that were subsequently names ILEs. The results of the search suggested that intron duplication is a widespread phenomenon in fungi. ILEs were associated with the majority of intron gains, suggesting that the other types of duplication (SGD and LCI) are of minor importance to the overall gains of introns. This was confirmed in a follow up study, where the authors investigated SGD and LCI in more detail. Altogether, the results suggest that ILEs are prevailing duplication events in fungi, explaining on average 76% of intron duplications. The data of the two studies support the hypothesis that ILEs' multiplication corresponds to the main mechanism of intron gain in fungi.

www.landesbioscience.com/journals/cib/article/23147

Reference

Collemare J, et al. Commun Integr Biol 2013; 6: e23147-1-5