OMICS Group Conferences
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International Conference & Exhibition on
Cell Science & Stem Cell Research

29 Nov - 1 Dec 2011 Philadelphia Airport Marriott, USA

Nuclear Ago2 regulates hATSCs survival through direct control of miR10b and SEPN1 expression

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Nuclear Ago2 regulates hATSCs survival through direct control of miR10b and SEPN1 expression; Argonaute 2 (Ago2) has a leading function in miRNA-induced RNA silencing, which is a conserved gene regulatory mechanism in cells and organisms. miRNAs are critical for stem cell self-renewal, development and other functions. We are reporting here that nuclear Ago2 directly controls human adipose tissue-derived stem cell (hATSC) survival in response to a critical dose of reactive oxygen species (ROS)-mediated oxidative cell damage or senescence by binding to a specific region of functional genes. The role of nuclear Ago2 has not been reported. Here, we show that human ATSCs in which Ago2 was downregulated underwent apoptosis. Silencing of Ago2 in hATSCs significantly induces upregulation of miR10b and miR23b expression. These mirs directly interfere with ROS scavenging gene expression, such as TXNL1 and GPX3. Upregulation of miR10b and miR23b is sufficient to induce hATSC cell apoptosis via p38 MAPK phosphorylation and Caspase 3 activation. In addition, Ago2 overexpression or interference of miR10b and miR23b expression in hATSCs partially rescued H_2O_2/ROS-mediated apoptotic cell death by upregulating TXNL2 and JUNK, Caspase 3, and cytochrome C expression. Nuclear Ago2-mediated miR10b and miR23b downregulation also allows cells to escape senescence, which results in TERT activation, stemness overexpression, and improved self-renewal and differentiation through Wnt5a/β-catenin activation. Ago2 expression is critical for stem cells to escape senescence through mir10b and mir23b downregulation. Ago2-binding gene Selenoprotein N1 (SEPN1) was also effectively involved in hATSCs' survival and self-renewal through ROS-mediated p38 MAPK inactivation.

Biography

Prof.Kang has been working in the field of adult stem cell research for 9-10 years. Before appointed as professor at SNU, she was Associate Professor at Pusan National University, Medical school in Korea after postdoctoral training at Tulane gene therapy center and National Primate Research Center in USA. Recently, her main interest in the field of stem cells is somatic cells or adult stem cells reprogramming into more pluripotent stem cells using nontoxic, novel small molecules or proteins. Prof. Kang is a member of the BrainKorea 21 Institute at the College of Veterinary Medicine at SNU, a graduate school to further excellence in training and also engaged in Korea Stem Cell Research Center in Korea as a creative member and main researcher.