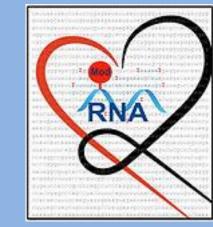


# The role and regulation of long noncoding RNA NEAT1 in vascular inflammation



Gayathri Rajesh Nair\* (170304157), Nikolaos Vlachogiannis, Simon Tual-Chalot, Aikaterini Gatsiou, Konstantinos Stellos BSc (Hons) Biomedical Genetics, Cardiovascular Disease Prevention & Resilience Hub, Institute of Genetic Medicine, Faculty www.StellosLab.com of Medical Sciences, Newcastle University, UK

g.nair@ncl.ac.uk

## **Background**

# **Atherosclerosis: an inflammatory disease** ADAR1

- Atherosclerosis is a chronic inflammatory disease of vessels. Accumulation of cholesterol and inflammation lead to formation of plaques on the inside surface of the vessels called atheroma.
- NEAT1, a long non coding RNA until recently considered "junk", has been found to accumulate at atherosclerotic plaques but its role remains unknown.

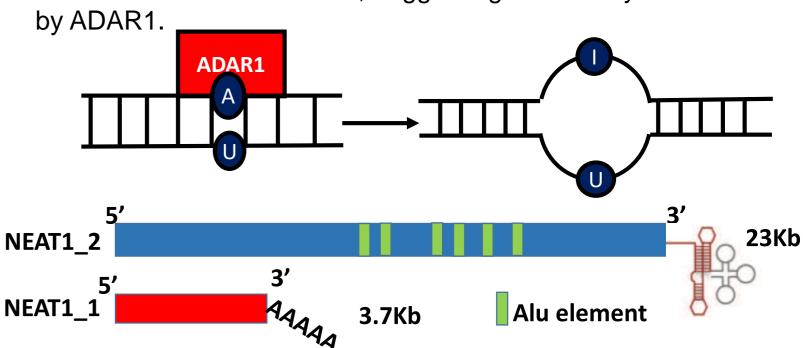
# **ADAR1** is increased in human atherosclerotic plaques **Atherosclerotic Normal artery** plaque negative

Stellos K et al, Nature Medicine, 2016

#### **ADAR1** may control **NEAT1** expression

The enzyme ADAR1 edits predominantly repetitive Alu elements, which comprise approximately 10% of the human genome.

NEAT1 has 6 Alu elements, suggesting that it may be modified



Adapted from T. Naganuma & Hirose, RNA Biol, 2013

# **Hypothesis and Aims**

#### **Hypothesis**

- NEAT1 controls the pro-inflammatory response in endothelial cells
- ADAR1 modifies NEAT1 Alu elements controlling NEAT1 expression

#### **Aims**

- > To study the role of NEAT1 in vascular inflammation
- > To examine the regulation of NEAT1 during pro-inflammatory conditions by ADAR1-mediated RNA editing

#### **Methods** Patients with: Stable Coronary Artery Disease Acute Coronary Syndrome siRNA lipofectamine Individuals without CAD Knocking down genes ADAR1/NEAT1 **Quantitative PCR:** measuring gene expression Peripheral blood mononuclear cells isolated 4h incubation from blood Reverse transcription, 42/44h incubation, RNA to cDNA ADAR1 and NEAT1 levels 5% CO2 measured 4/6h incubation, **RNA** extraction TNFα treatment 5% CO2 Statistical Analysis 20ng/ml

#### **NEAT1** in endothelial cell inflammatory response

control

#### **Knocking-down NEAT1 reduces endothelial inflammatory response** 3000-2000-200 1000-100-Scrambled siNEAT1 Scrambled siNEAT1 **Scrambled siNEAT1** TNF $\alpha$ treatment (4h) TNF $\alpha$ treatment (4h) TNF $\alpha$ treatment (4h) (20ng/ml) (20ng/ml) (20ng/ml) ange from baseline) 30000expression 20000-ICAM1 (fold cha E-selectii (fold cha (fold cha ວິ 100-9**T**I Scrambled siNEAT1 Scrambled siNEAT1 Scrambled siNEAT1 TNF $\alpha$ treatment (4h) TNF $\alpha$ treatment (4h) TNF $\alpha$ treatment (4h) (20ng/ml) (20ng/ml) (20ng/ml) ADAR1 mRNA expression (fold change from baseline) 0 0 1 1 0 5 0 2 0 5 NEAT1 IncRNA expression (fold change from baseline) 0.5-**Scrambled** siADAR1 scrambled siADAR1 scrambled scrambled TNFα 6hours (20ng/ml) TNFα 6hours (20ng/ml)

## Conclusion

- Long noncoding RNA NEAT1 plays a role in driving pro-inflammatory response in endothelial cells.
- ADAR1 controls NEAT1 expression in endothelial cells.

## ADAR1 and NEAT1 in human atherosclerotic heart disease

