Therapeutic applications of SAMMSON IncRNA inhibition in uveal melanoma

Shanna Dewaele1,2, Katrien Vanderheyden1,2, Boel De Paepe3, Fariba Nemati4, Sergio Roman Roman4, Rudy Van Coster3, Jo Vandesompele1,2 and Pieter Mestdagh1,2

1 Center for Medical Genetics, Ghent University, Ghent, Belgium
2 Cancer Research Institute Ghent (CRIG), Ghent University, Ghent, Belgium
3 Department of Pediatrics, Division of Pediatric Neurology and Metabolism, Ghent University Hospital, Ghent, Belgium
4 Translational Research Department, Institut Curie, PSL Research University, Paris, France

INTRODUCTION

- Most common eye tumor in adults
- Primary treatment: 5x or Rx
- Metastatic disease → survival time < 12 months
- No treatment for metastatic disease
- Melanoma specific IncRNA SAMMSON

OBJECTIVE

- Validation of the therapeutic effects of SAMMSON inhibition in uveal melanoma
- Evaluation of the effects of SAMMSON inhibition on mitochondrial respiration
- Validation of combination therapy including SAMMSON inhibition and MEK inhibition

RESULTS

SAMMSON knock down using LNA antisense oligonucleotides reduces cell viability and induces cell apoptosis

SAMMSON knock down results in a decreased mitochondrial respiration

Combining SAMMSON inhibition and MAPK inhibition results in a synergistic decrease in cell viability

SAMMSON inhibition as monotherapy and in combination with MEK inhibition reduces tumor growth in vivo

CONCLUSION

- SAMMSON knockdown results in
  - Reduction in cell viability and induction of apoptosis
  - Decreased mitochondrial respiration
  - Decreased tumor volume in vivo
- SAMMSON inhibition synergizes with MEK inhibition

FUTURE DIRECTIVES

- Identification of SAMMSON interaction partners
- Validation of the observed phenotype using alternative ASOs
- Combination therapy of SAMMSON inhibition with PKC inhibitors