PLASMA NUCLEIC ACIDS AS POTENTIAL PREDICTORS OF STATIN ASSOCIATED MUSCLE SYMPTOMS

Pilot study

J.A. Hubáček

P. Hucková, D. Dlouhá, V. Adámková. M. Vrablík

IKEM +

1.MF, CU, General Hospital

Prague

Statins

- **3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors**
- **Among the most commonly prescribed drugs**
  - (US - 17% of adults aged 40–59, 48% of adults older than 75)
- **Treatment**
  - **High plasma cholesterol**
  - **Prevention of CVD**
- **Other potential profits discussed**

Statins and undesirable side effects of treatment

- Low frequency, but high absolute number (enormous prescription)
- 2 - 10% of subjects
- New onset of diabetes
- Increased liver enzymes
- Autoimmune diseases (Crohn d., myasthenia, asthma,…)
- Statin-Associated Muscle Symptom (SAMS)
  - myalgia
  - myopathy
  - rhabdomyolysis

Markers of SAMS

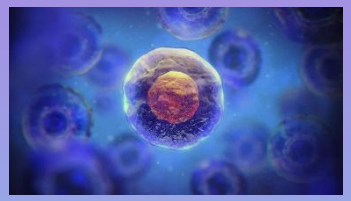
?

no validated biomarkers or tests that can be used to predict/confirm SAMS

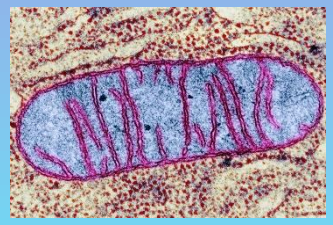
(…creatine kinase…)

Cell free nucleic acids in plasma

- cf DNA
  - nucleus
  - mitochondril



Released form damaged cells



- miRNA (regulatory)
  - Muscle specific
  - More stable

Short fragments
Short half life

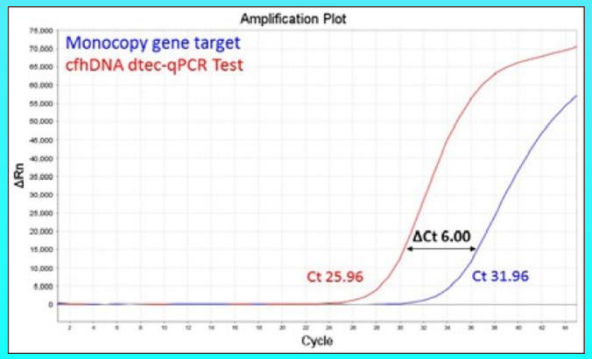
? New markers of SAMS ?

Would it be possible to use
cell free nucleic acids
to predict
SAMS

Methods

- 17 subjects, MI survivors
  - 1st sample „statin free“
  - 3 samples on statins
  - 7 reported muscle problems/discomfort

- 2 nDNA markers
- 2 mtDNA markers
- 3 muscle specific miRNA (133a-3p; 1-3p; 23a-5)



- qPCR
- Unadjusted relative comparison

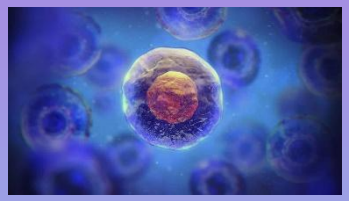
Results

- Absolute concentrations
  - cfnDNA (400-2 000 copies per mL)
  - cfmtDNA (1 000-1 000 000 copies per mL)
  - miRNA (100-10 000 copies per mL)

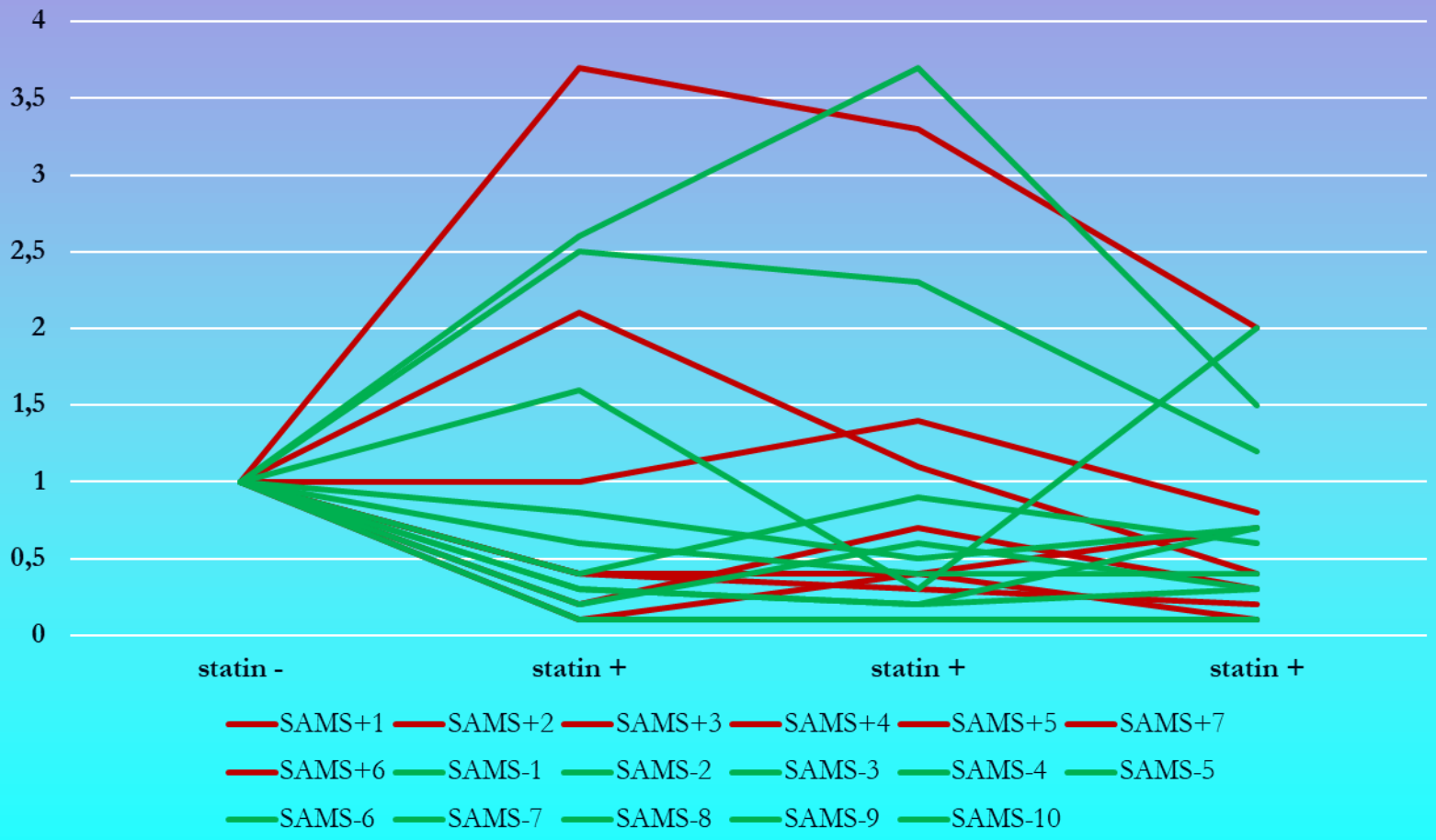
remember the length differences!!

- Relative concentrations
  - 1st point = 1

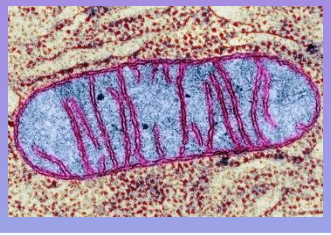
cfnDNA



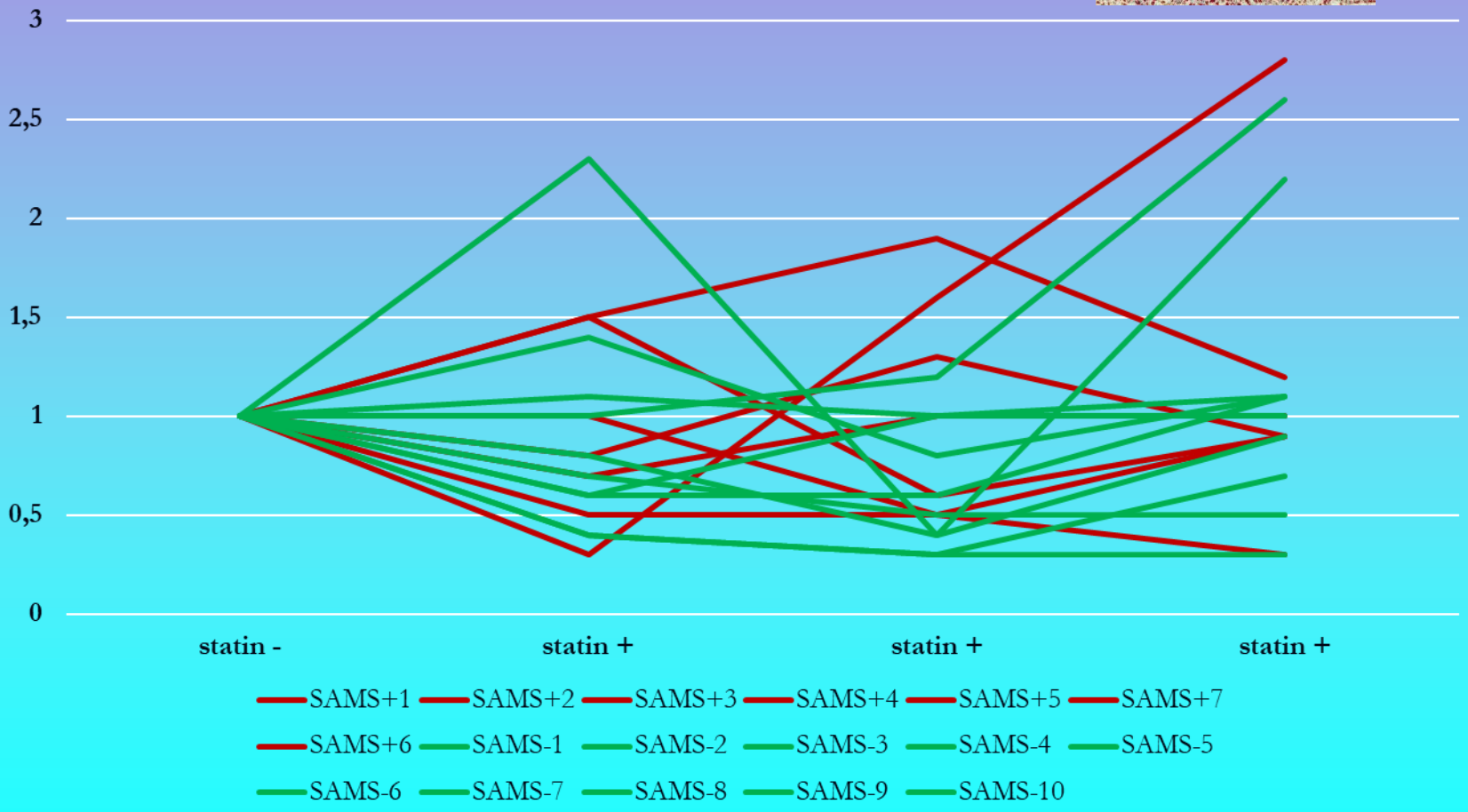
Relative concentrations



cfmtDNA



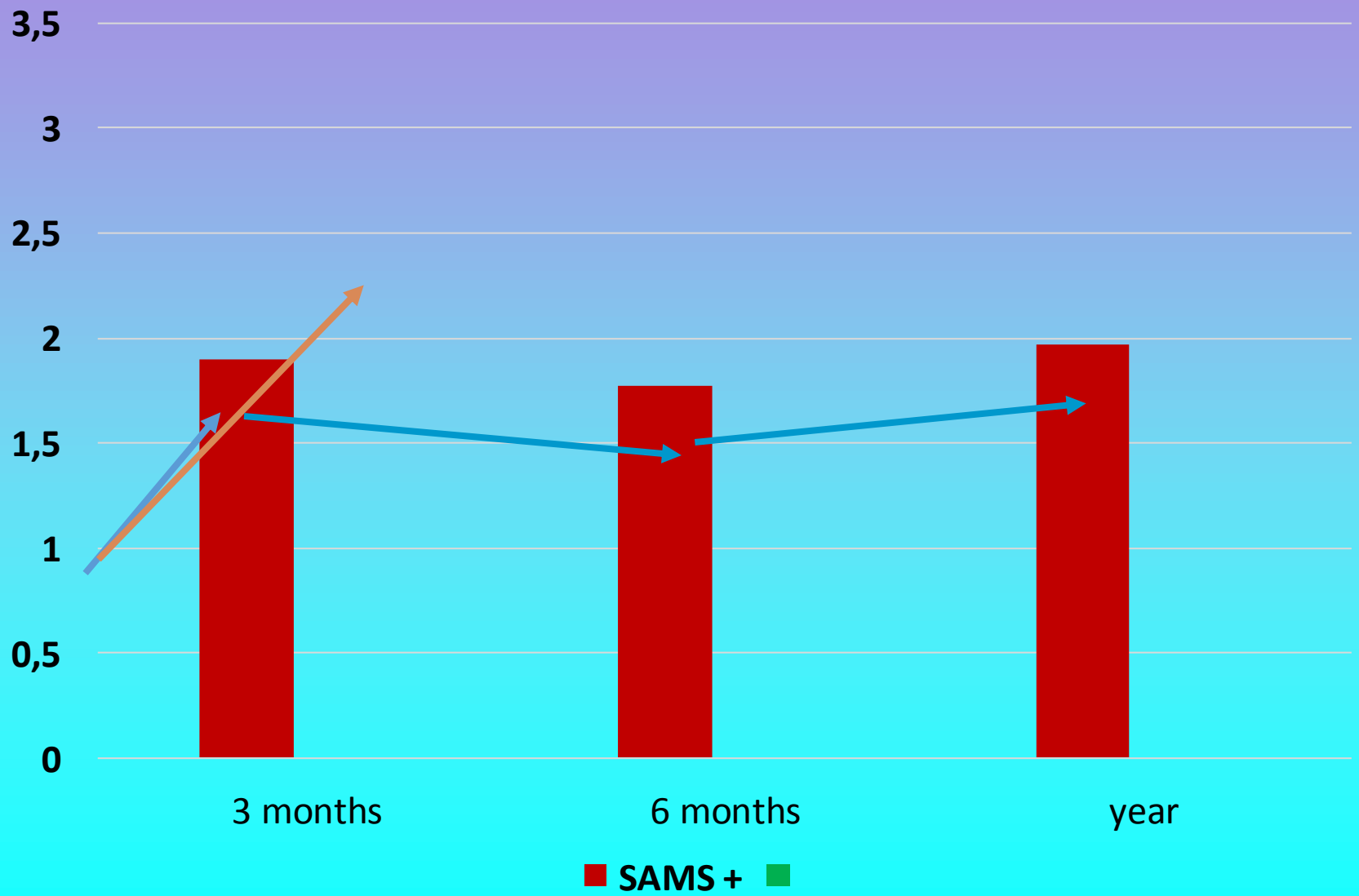
Relative concentrations



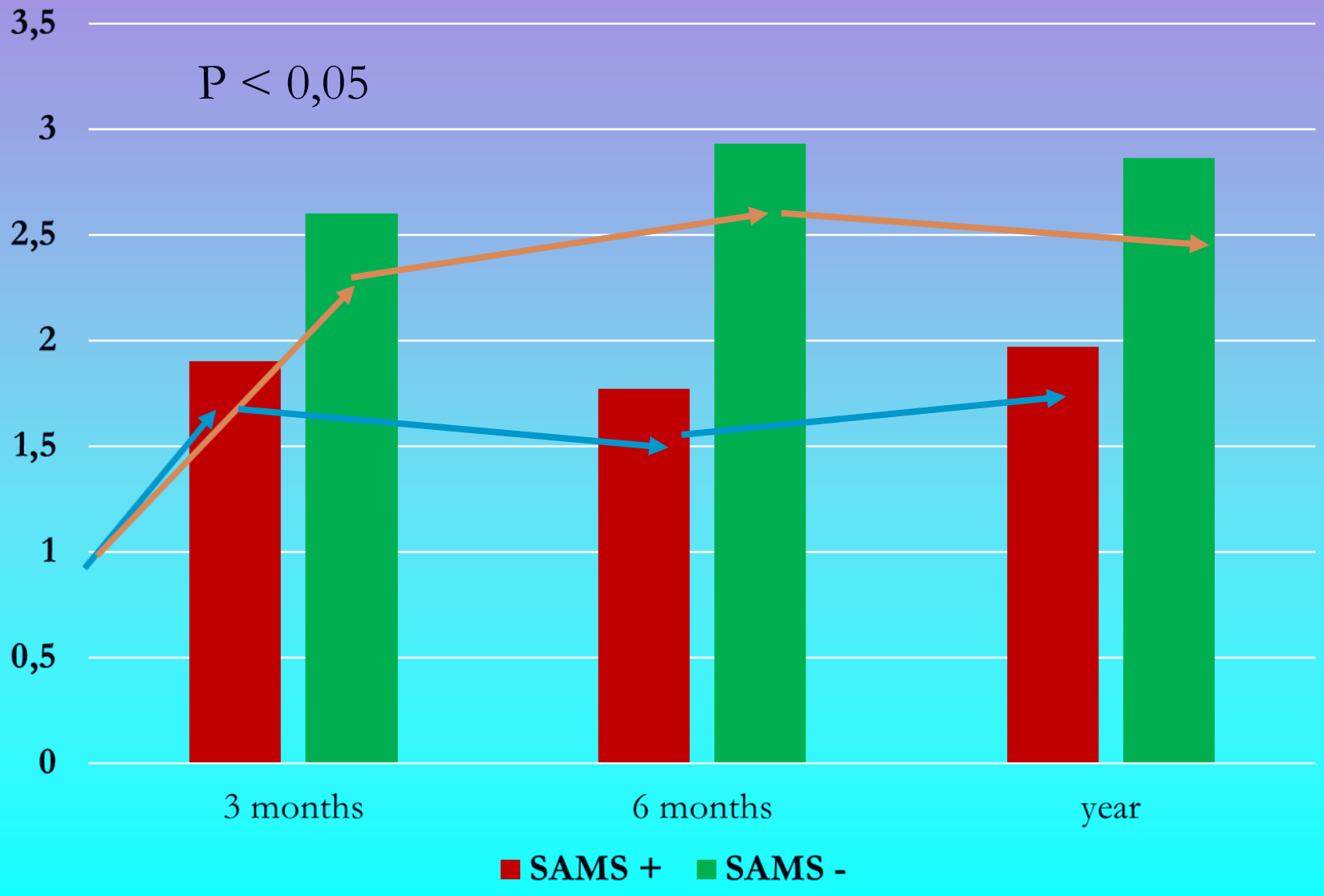
miRNA

- More promising…?
  - miRNA 133a-3p P < 0,05
  - miRNA 1-3p n.s.
  - miRNA 23a-5 P = 0,05

miRNA 133a-3P



miRNA 133a-3P



Potential confounders

- Physical activity performed
- Smoking
- Injuries
- Sample handling and storage

- Independent on
  - Age
  - Gender
  - Food intake

Conclusions

- cfnDNA and cfmtDNA seems not to be strong promising predictors of SAMS
- …other groups of subjects needed…

Complicated and heterogeneous

- miRNA
- unexpected increase of concentrations in unaffected subjects
- improper miRNA regulation?

Thanks for your attention!