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THE EFFECT OF SGA_s ON ADIPOCYTE GLUCOSE UPTAKE DURING SHORT-TERM INCUBATIONS

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March 16th 2018

Background

Schizophrenia facts:

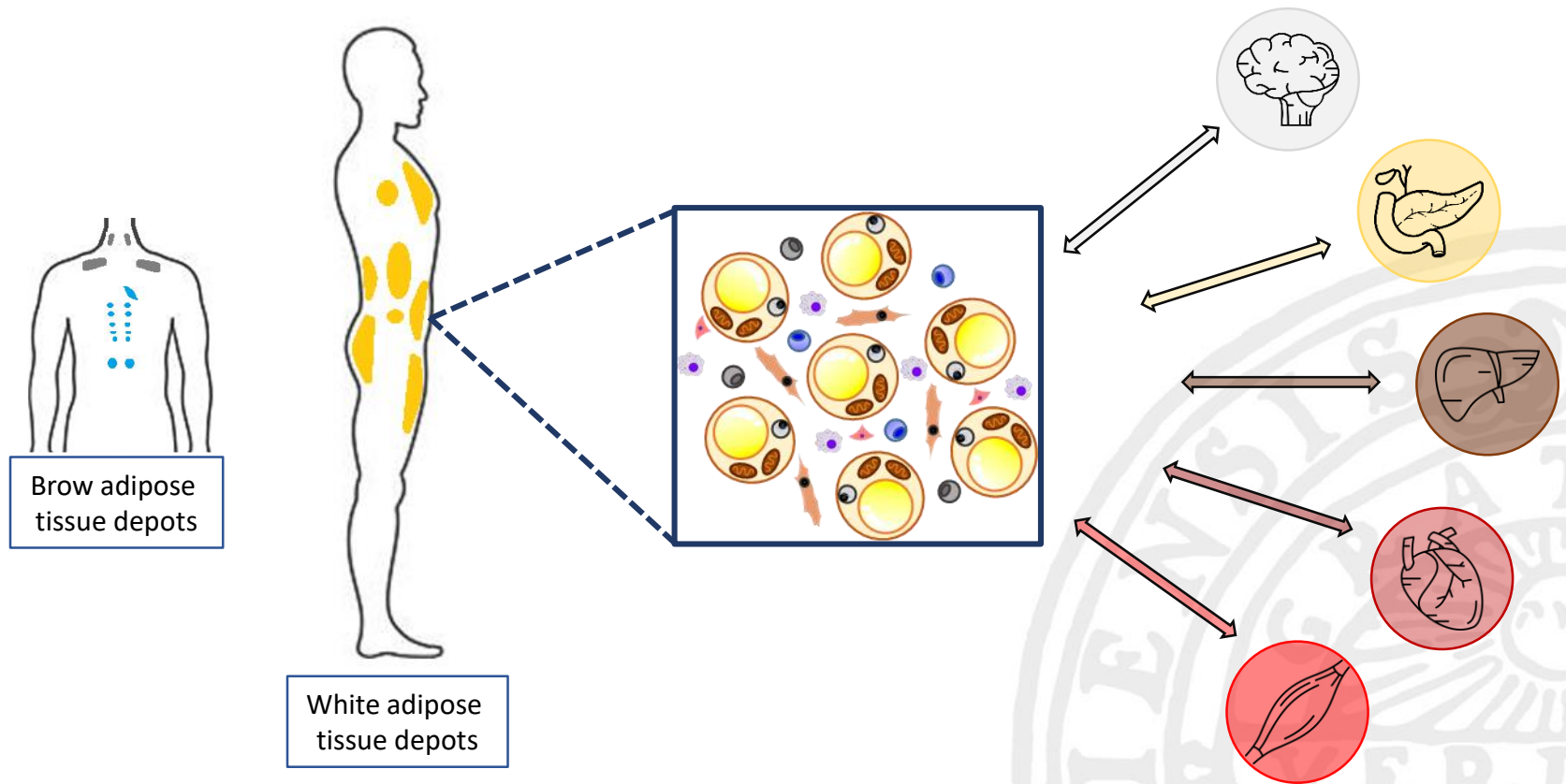
- 21 million people worldwide
- Obesity 45-55%
- Type 2 Diabetes 10-15 %

Olanzapine presents a high risk of developing metabolic changes: higher glucose, Triglycerides and cholesterol levels in plasma.

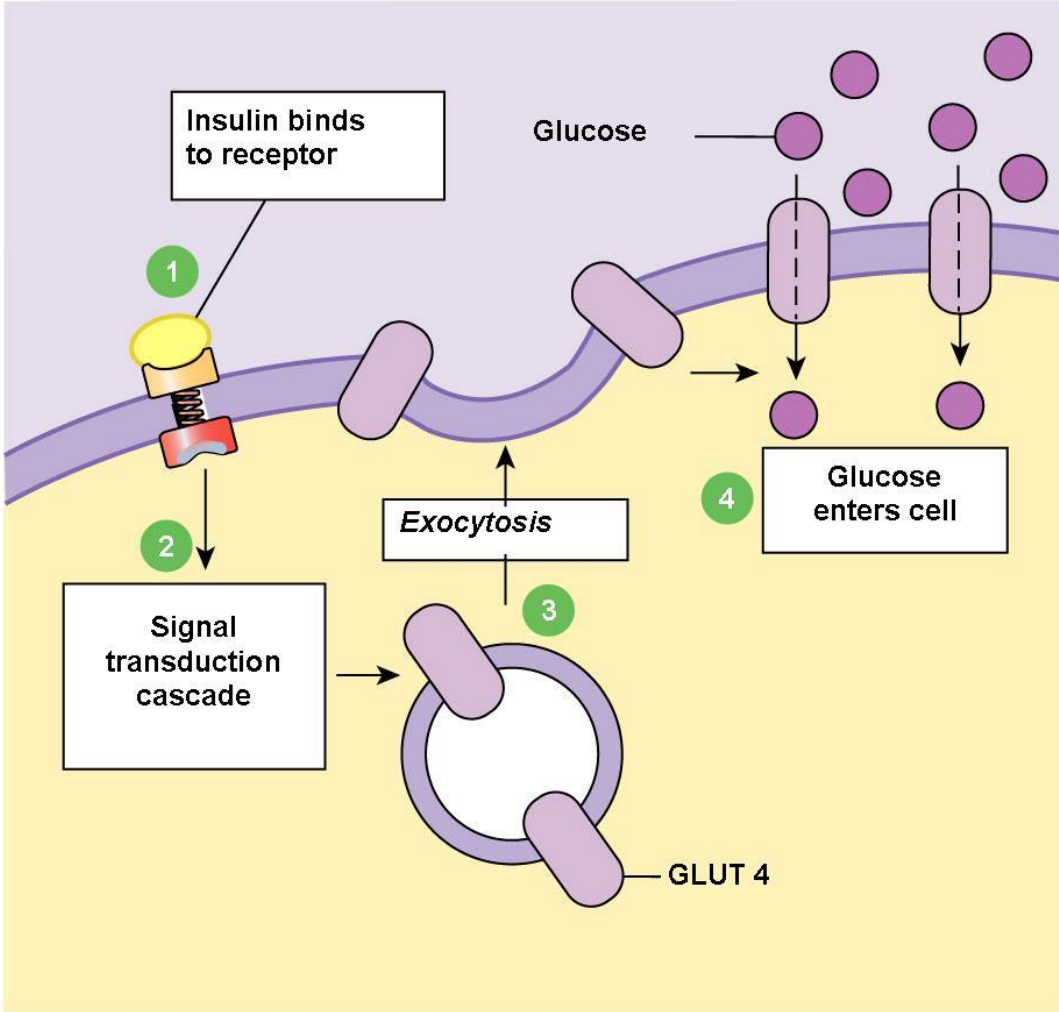
Aripiprazole has the opposite effect even reducing weight.

Hypothesis: Glucose elevation is justified by acute alteration in insulin signalling in adipocytes, altering Glucose uptake.

Adipose tissue



Glucose Uptake

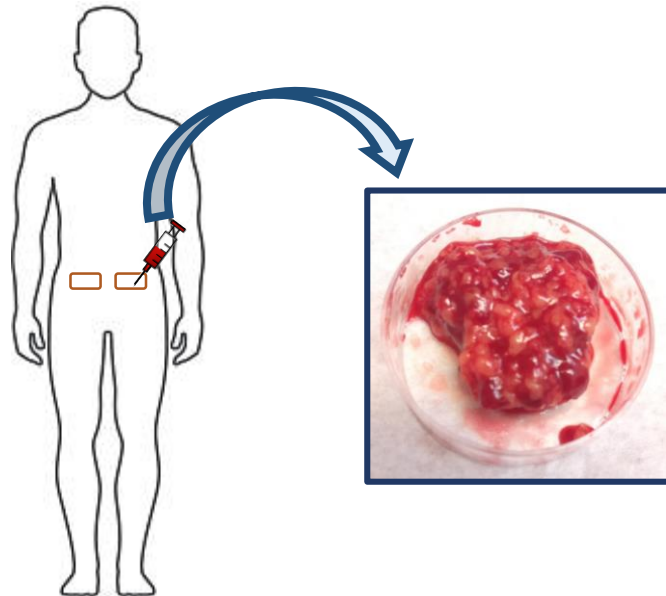


Concentrations being tested and therapeutic plasma concentrations observed in humans

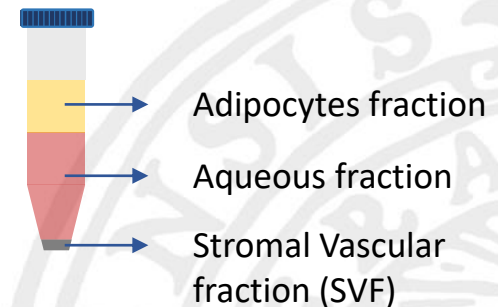
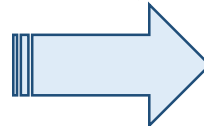
Total plasma concentrations (μM) after steady state		
	Low dosage	High dosage
Olanzapine	0.07	0.2
Aripiprazole	0.2	0.95

Concentrations tested (μM)						
Olanzapine	0.004	0.04	0.1	0.2	2	20
Aripiprazole	0.02	0.2	0.5	1	10	100

Experimental design

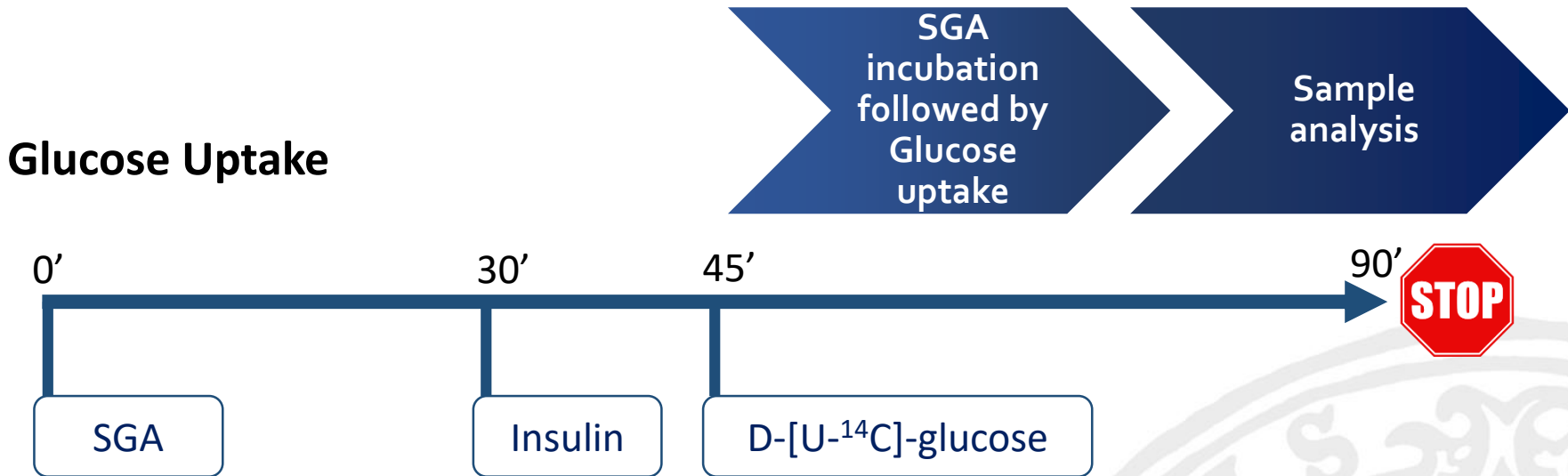


~1h incubation with collagenase



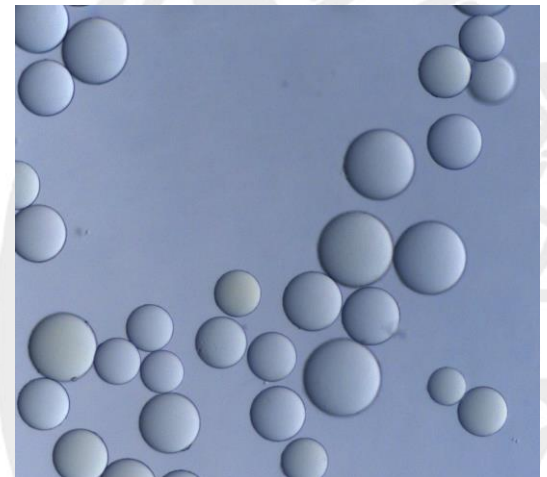
- Heathy volunteers
- Fasting
- Not taking antipsychotics or antidepressants

Experimental design

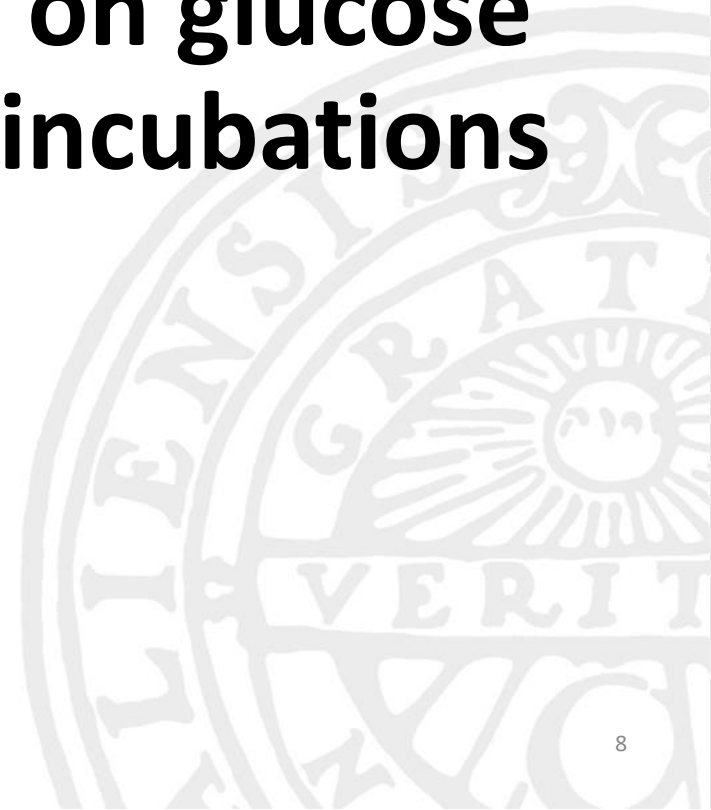


Cell number:

- Cell Size
- TG content



Results of SGAs effect on glucose uptake for short term incubations



Olanzapine

	Mean and SD
N	8
BMI (kg/m ²)	26.3 ± 3.6
Fasting Glucose (mmol/L)	5.9 ± 0.6
Hba1C (mmol/mol)	35 ± 4
Insulin (mE/L)	7.9 ± 2.5
Waist/Hip	0.84 ± 0.07
Age (years)	32 ± 13

Dose response Curve for Olanzapine

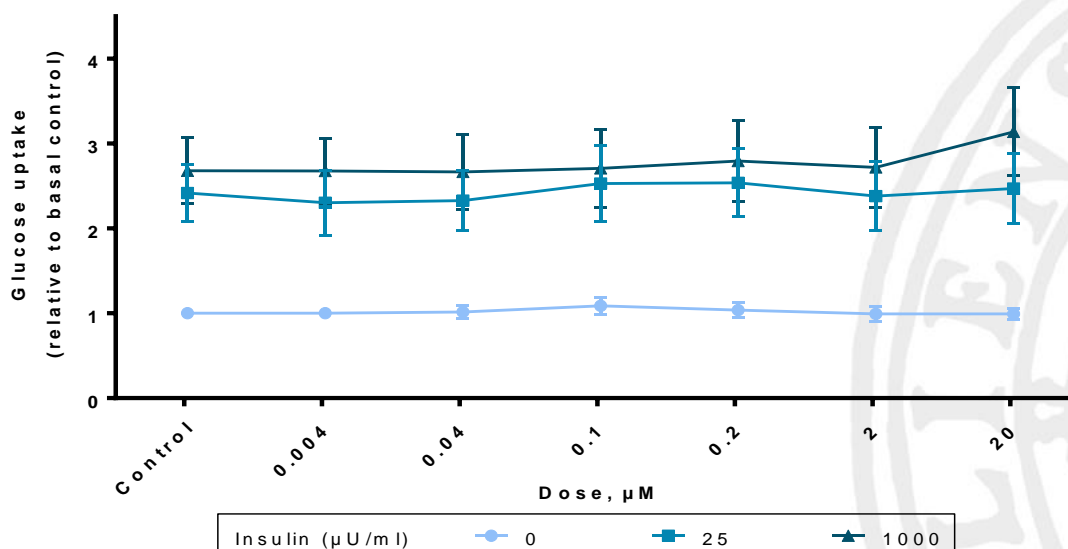


Fig 1 – Dose response curve for olanzapine effect on adipocyte glucose uptake. Mean \pm S.E.M are shown. Statistical analysis: Paired t-test. No statistical difference observed.

Aripiprazole

	Mean and SD
N	7
BMI (kg/m ²)	25.1 ± 2.8
Fasting Glucose (mmol/L)	5.7 ± 0.6
Hba1C (mmol/mol)	34 ± 3
Insulin (mE/l)	8.6 ± 2.5
Waist/Hip	0.9 ± 0.1
Age (years)	47 ± 22

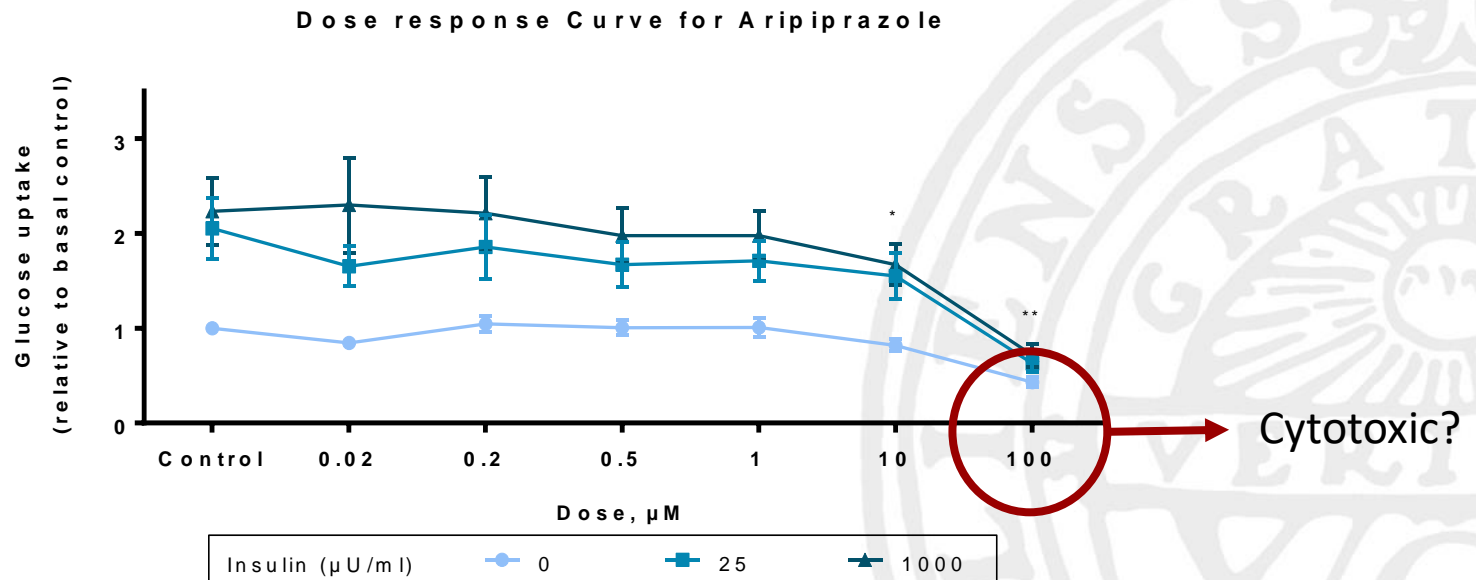


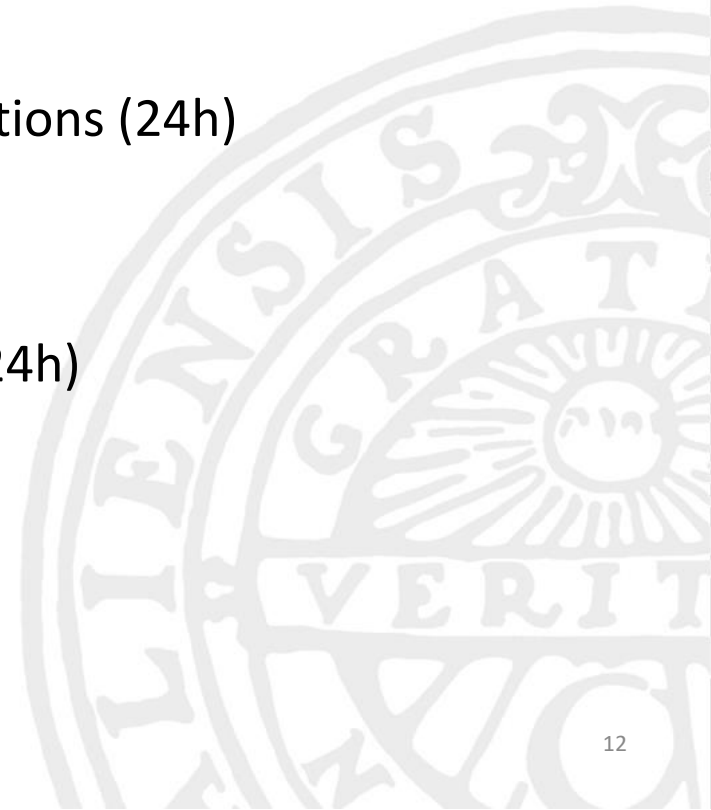
Fig 2 – Dose response curve of aripiprazole effect on adipocyte glucose uptake. Mean ± S.E.M are shown. Statistical analysis: Paired t-test. * p<0.05; ** p<0.01.

Conclusions

- Short-term incubations with olanzapine do not affect adipocyte glucose uptake in the concentrations tested.
- Short-term incubations with aripiprazole do not affect adipocyte glucose uptake for the exception of supra therapeutic concentrations, 10 and 100 μM .
- **At therapeutic concentrations, tested SGAs appear to have no effect on insulin signaling in short incubations!!**

Future work

- Viability assays for the concentrations tested
- Measure Glucose uptake in long term incubations (24h)
- Measure Lipolysis in long term incubations (24h)



Acknowledgements:

Jan Eriksson

Maria João Pereira

Gretha Boersma

Assel Sarsenbayeva

Prasad Kamble

Xesus Abalo

Kristina Almby

Petros Katsogiannos

Anna Ehrenborg

Sofia Löfving

Monika Gelotte

Caroline Woxberg

All medical personnel

Thank you!