



7. KONFERENCA UČITELJEV/-IC NARAVOSLOVNIH PREDMETOV – NAK 2023:
**Z ZNANJEM IN RAVNANJEM NASLAVLJAJMO
PODNEBNE SPREMEMBE IN TRAJNOSTNOST**
17. DO 18. APRIL 2023, LAŠKO

Sladkorna bolezen tipa 2: kaj se lahko naučimo iz živalskih modelov

Jurij Dolenšek, Maša Skelin Klemen in Andraž Stožer



REPUBLIKA SLOVENIJA
MINISTRSTVO ZA OKOLJE,
PODNEBJE IN ENERGIJO



REPUBLIKA SLOVENIJA
MINISTRSTVO ZA VZGOJO IN IZOBRAŽEVANJE

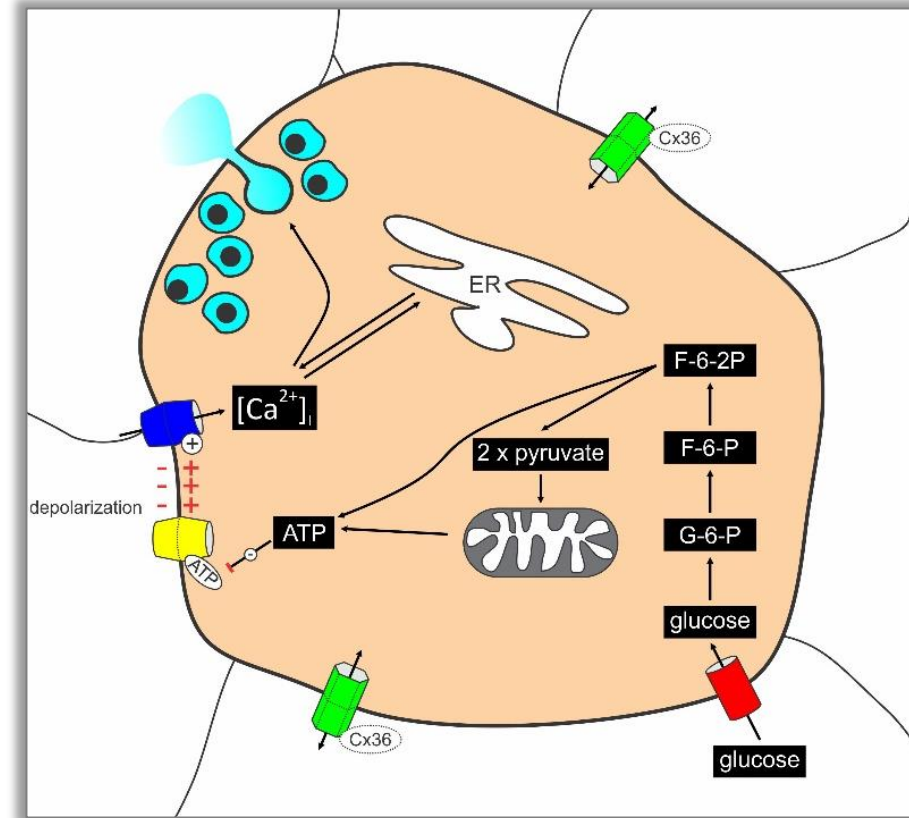
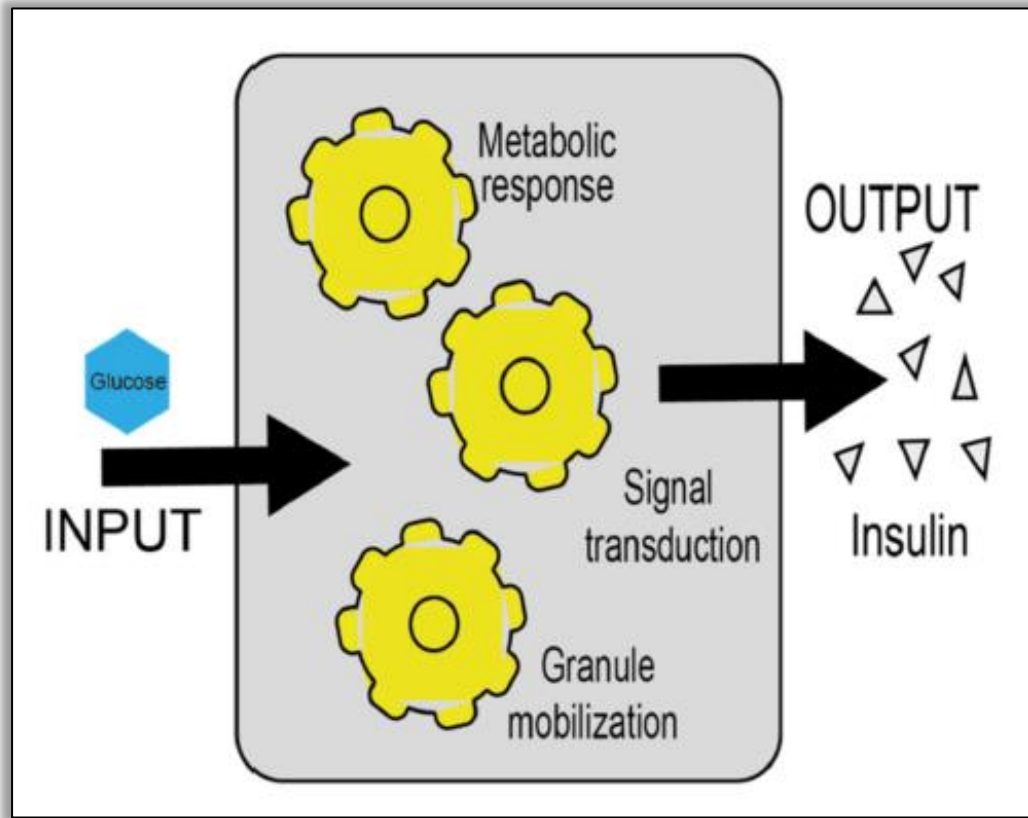


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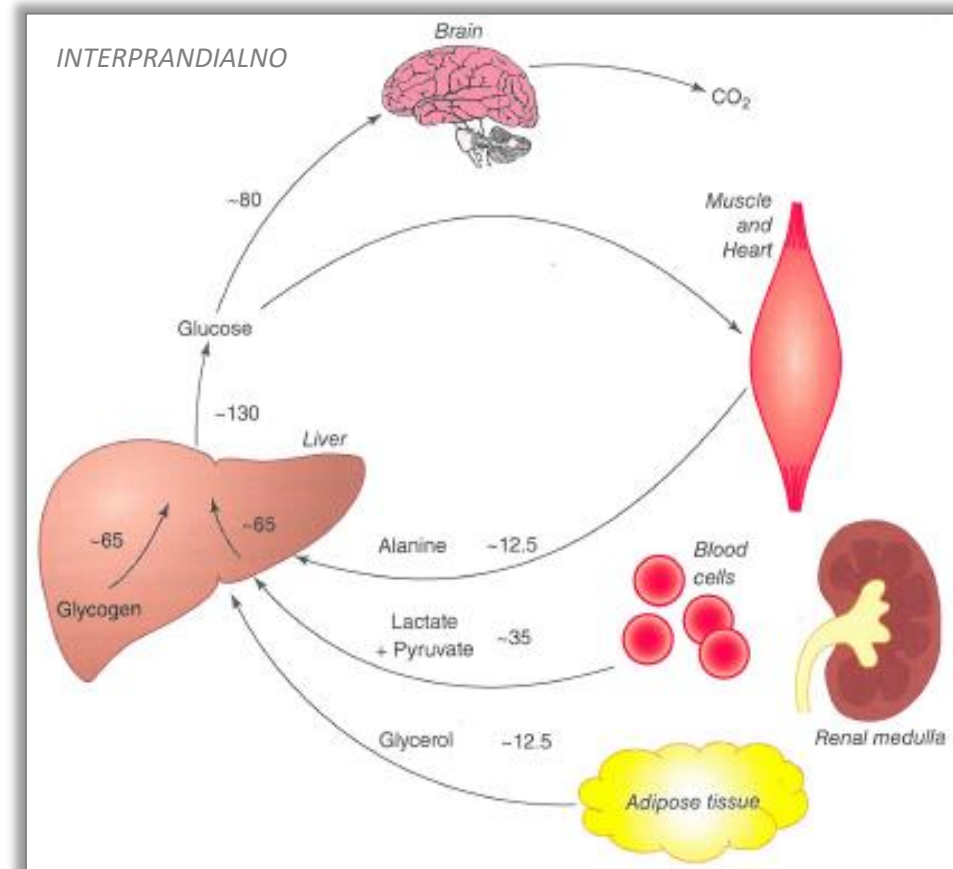
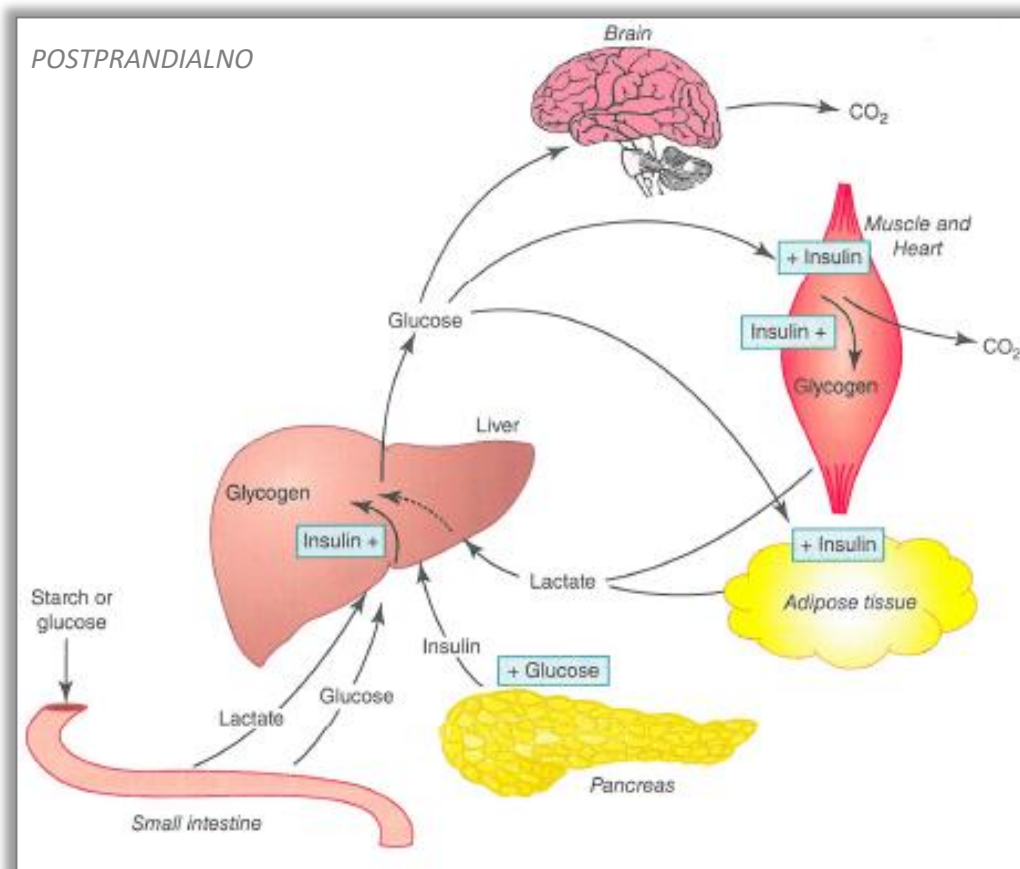
Dogodek delno financira Ministrstvo za okolje, podnebje in energijo s sredstvi Sklada za podnebne spremembe, v okviru projekta Podnebni cilji in vsebine v vzgoji in izobraževanju.



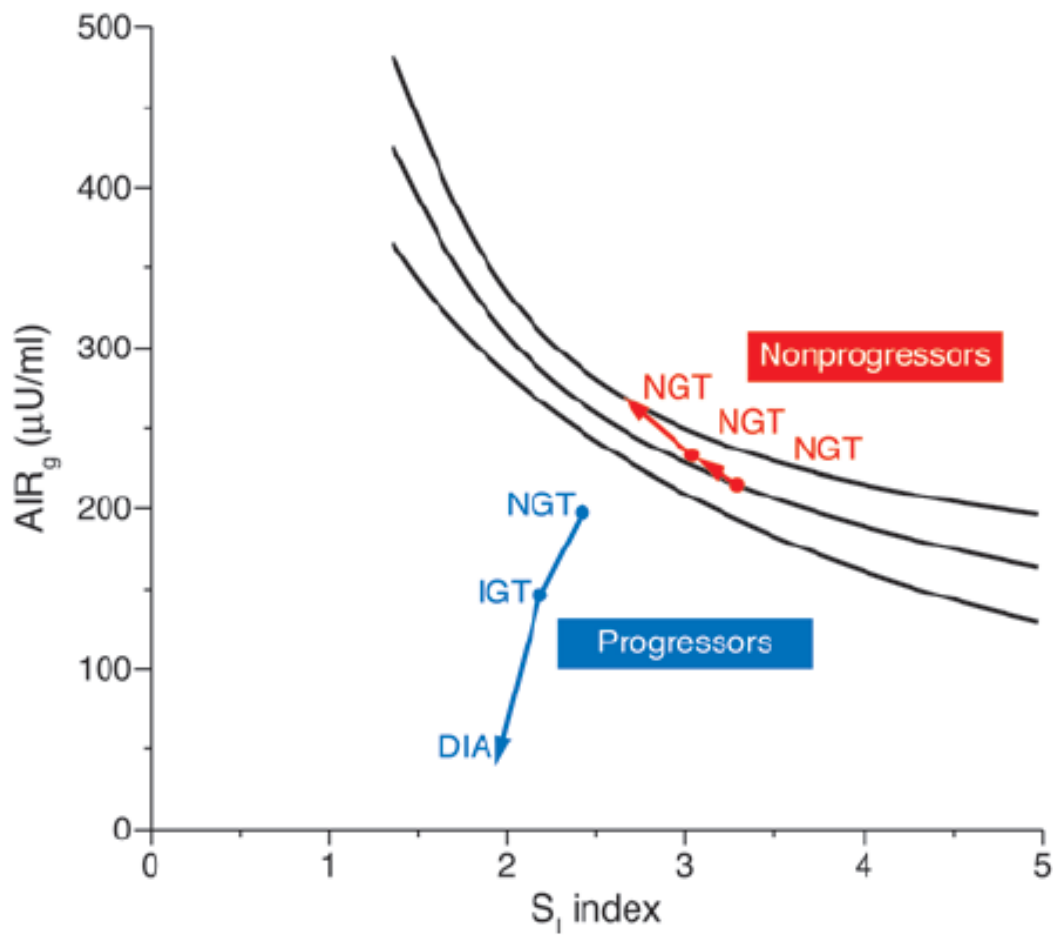
Langerhansovi otočki: Funkcija



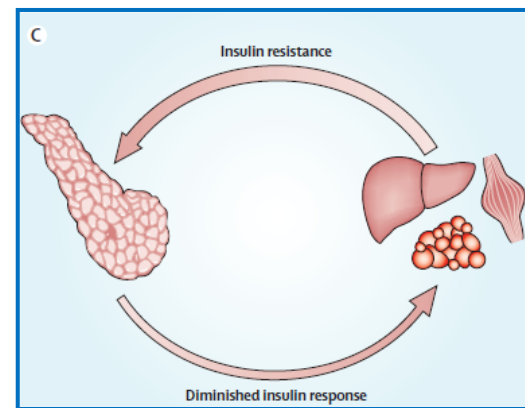
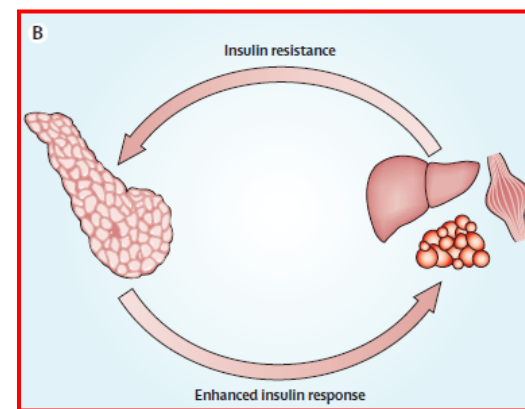
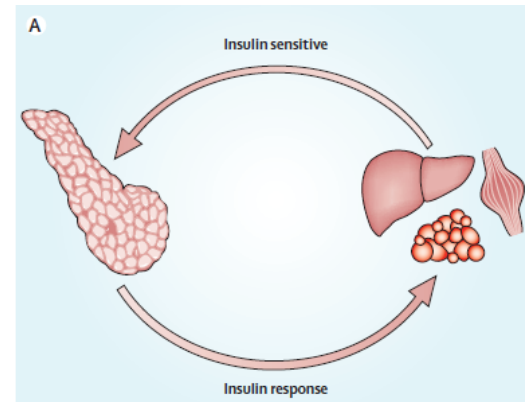
INZULIN: učinek *in vivo*



Etiopatogeneza sladkorne bolezni



Kahn Diabetologia 2003



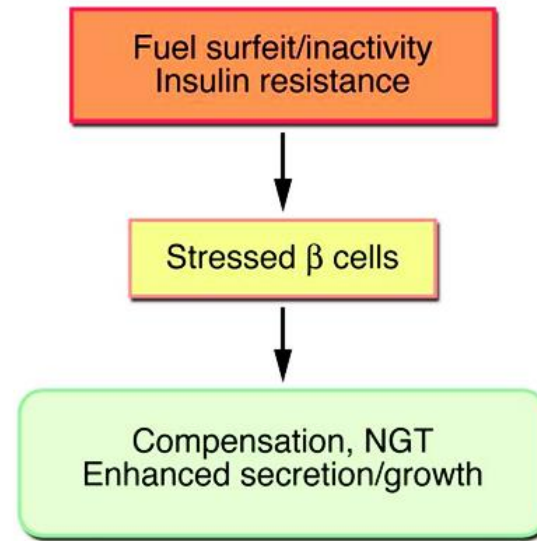
Kahn, Lancet 2014



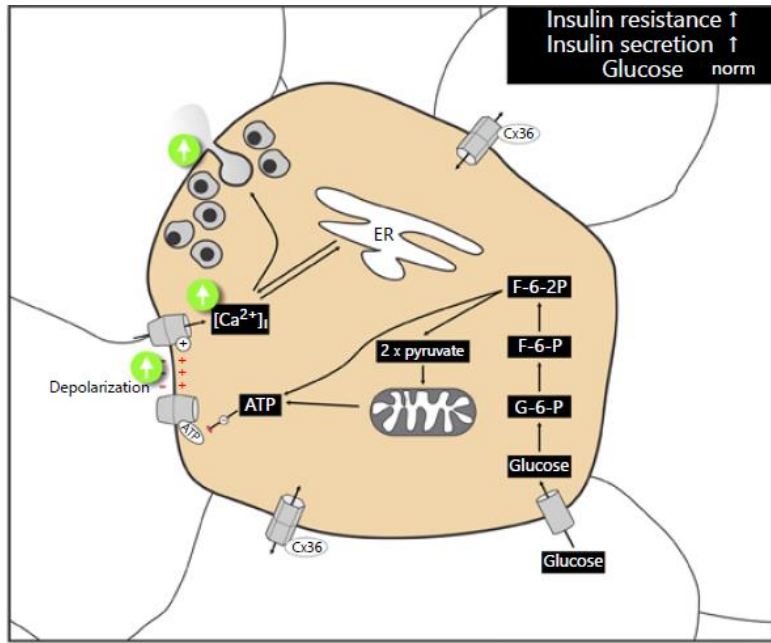
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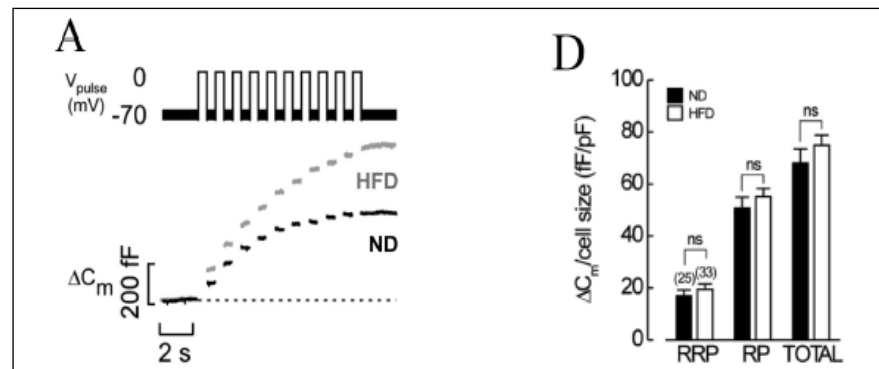
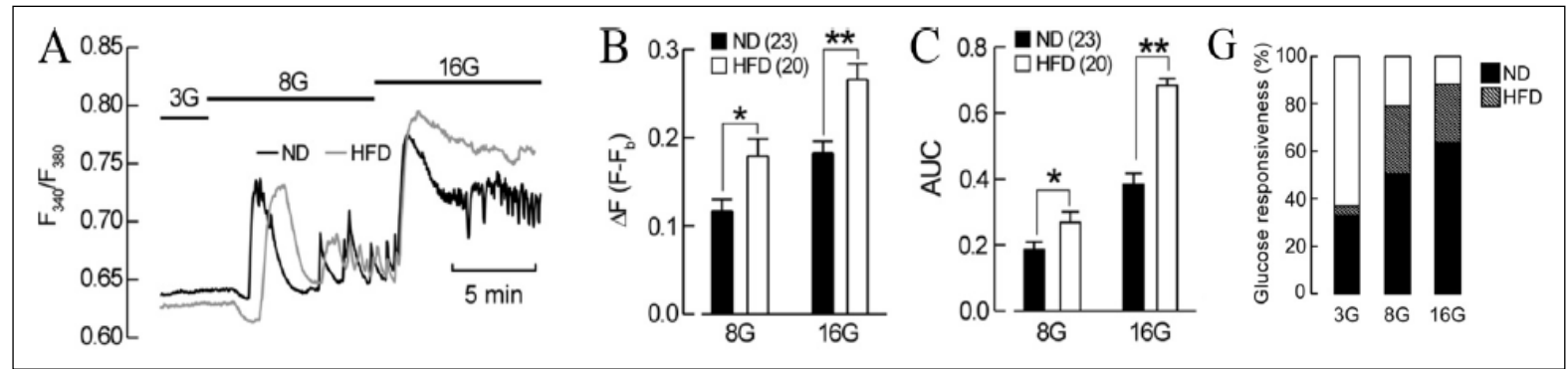
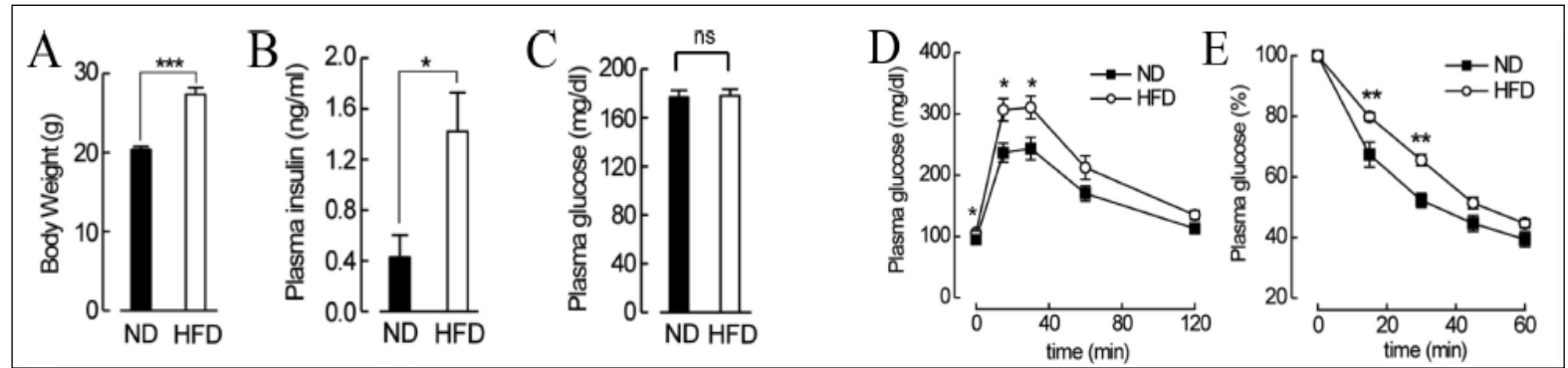
Etiopatogeneza sladkorne bolezni



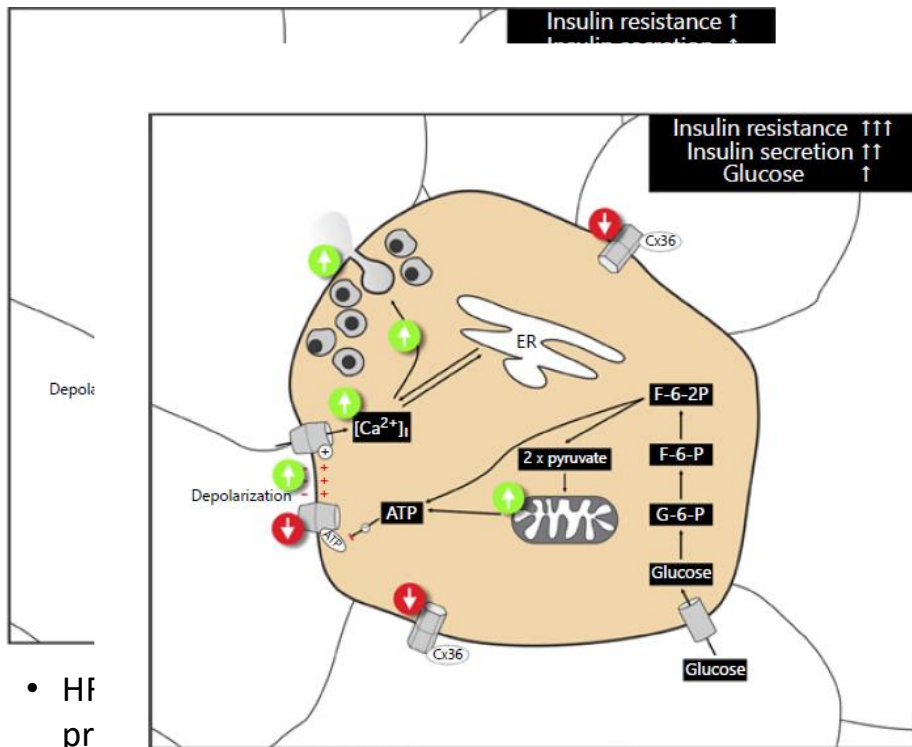
Etiopatogeneza sladkorne bolezni: POPOLNA KOMPENZACIJA



- HFD-fed female mice, probably IR/NGT humans
- Left-shifted dose-response curve
- IR, normoglycemia, normal 2h ipGTT
- Increased insulin secretion

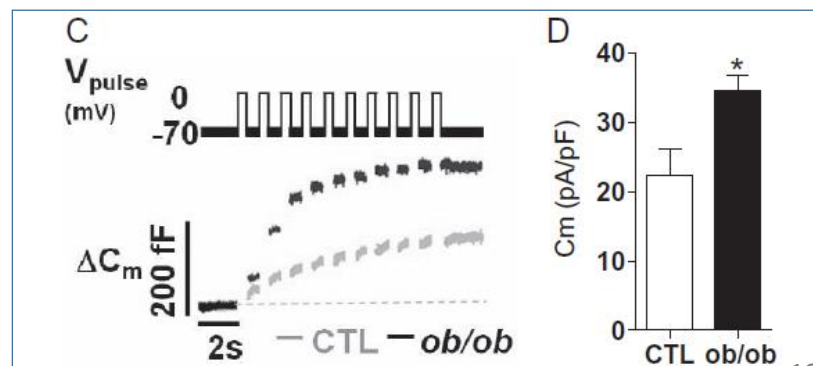
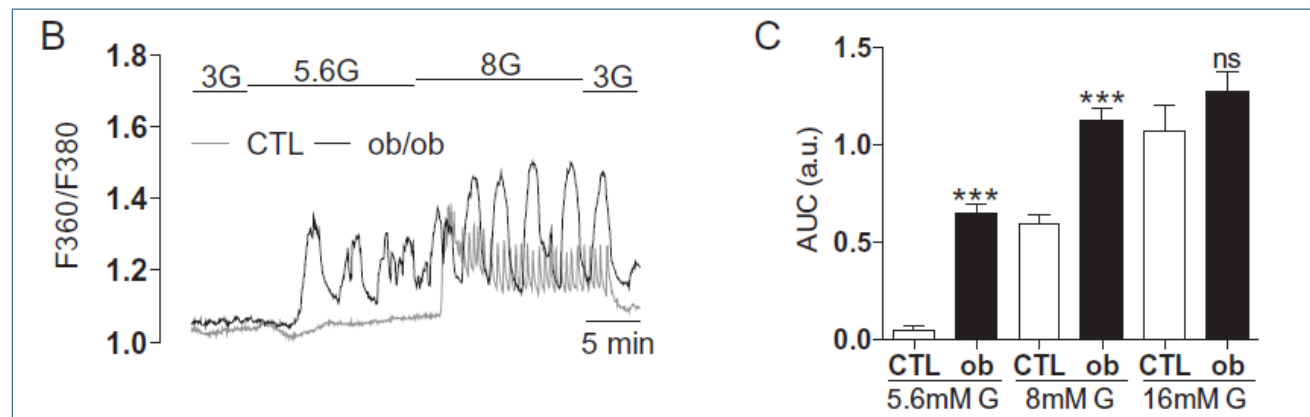
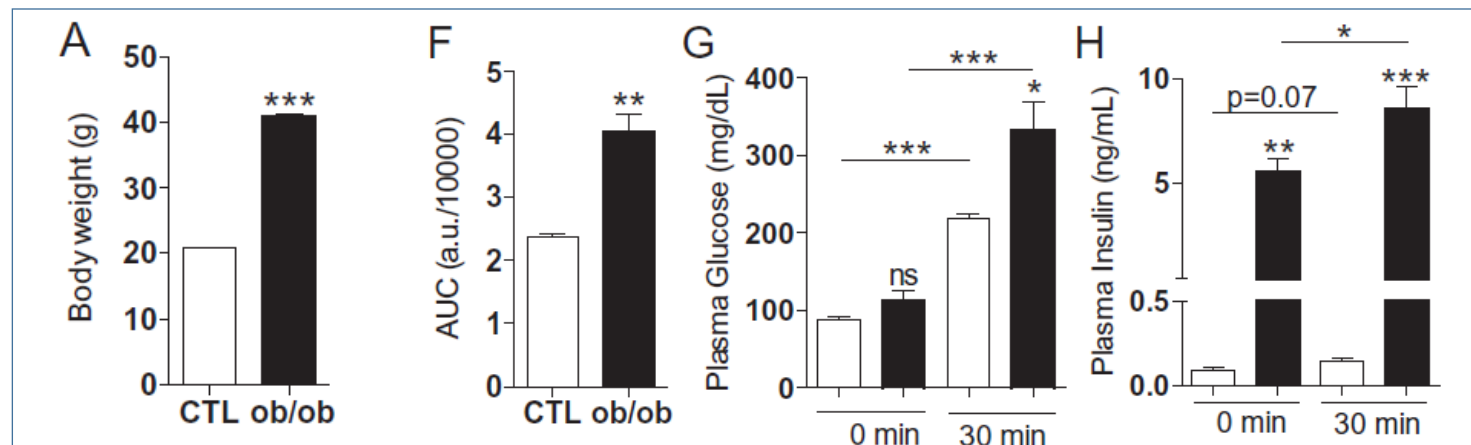


Etiopatogeneza sladkorne bolezni: DELNA KOMPENZACIJA

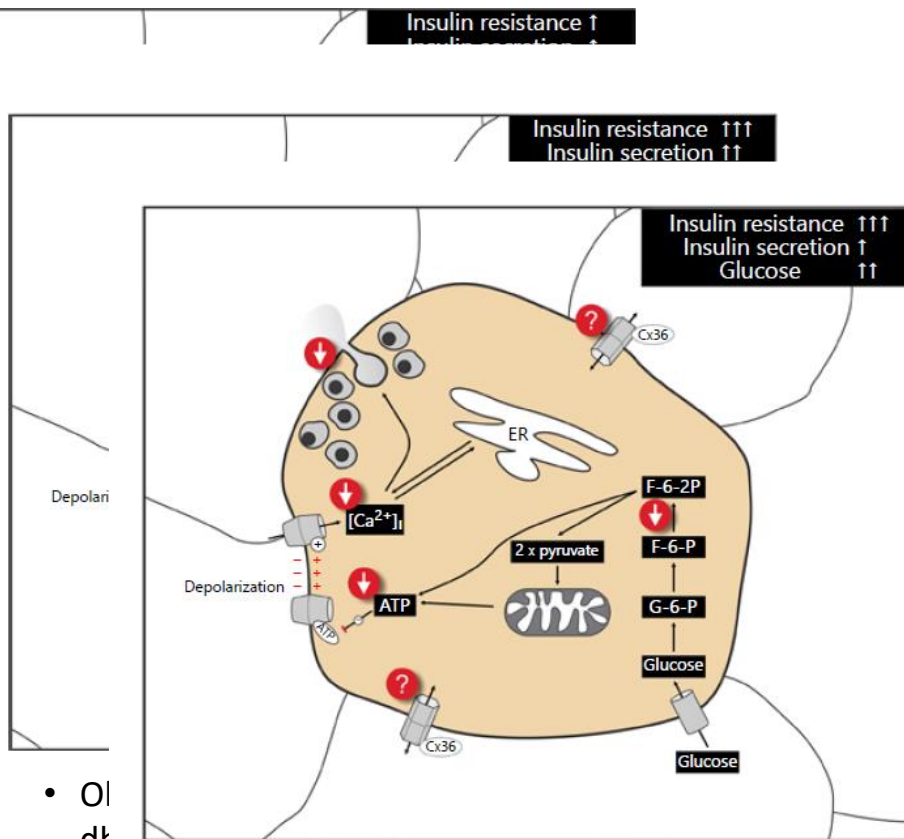


- HF
- pr
- Le
- cu
- IR,
- 2h
- In

- Ob/ob mice, HFD-fed male mice, young db/db mice, probably IR/IGT/IFG humans
- Left-shifted dose-response curve
- Hyperglycemia or increased 2h ipGTT
- Further increased insulin secretion
- Impaired intercellular coupling or other parameters

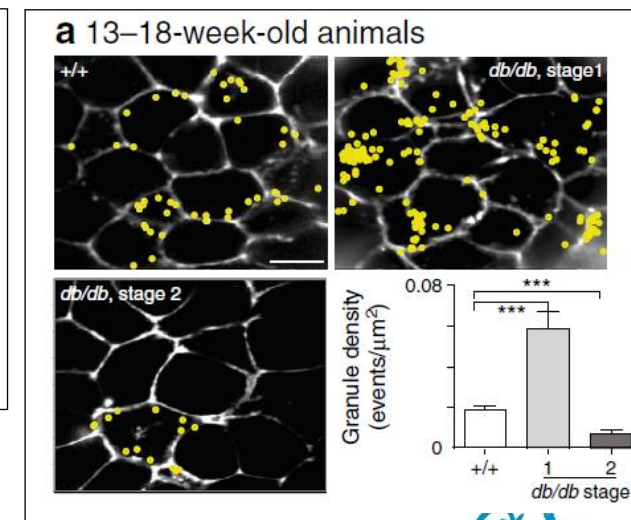
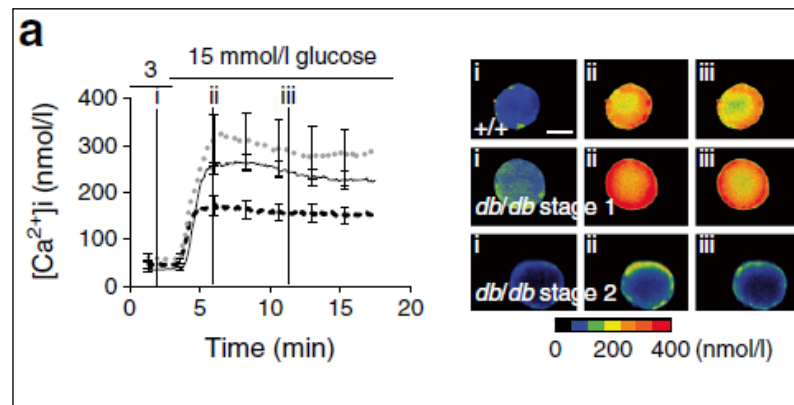
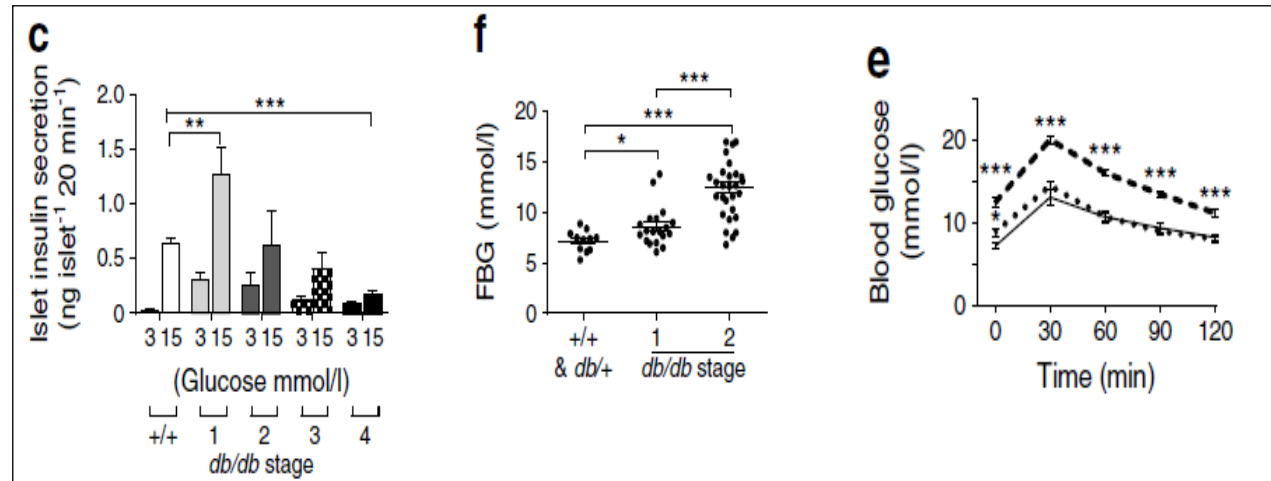


Etiopatogeneza sladkorne bolezni: DEKOMPENZACIJA



- Hf
- pr
- Le
- cu
- IR,
- 2h
- In
- Ol
- dk
- Le
- Hy
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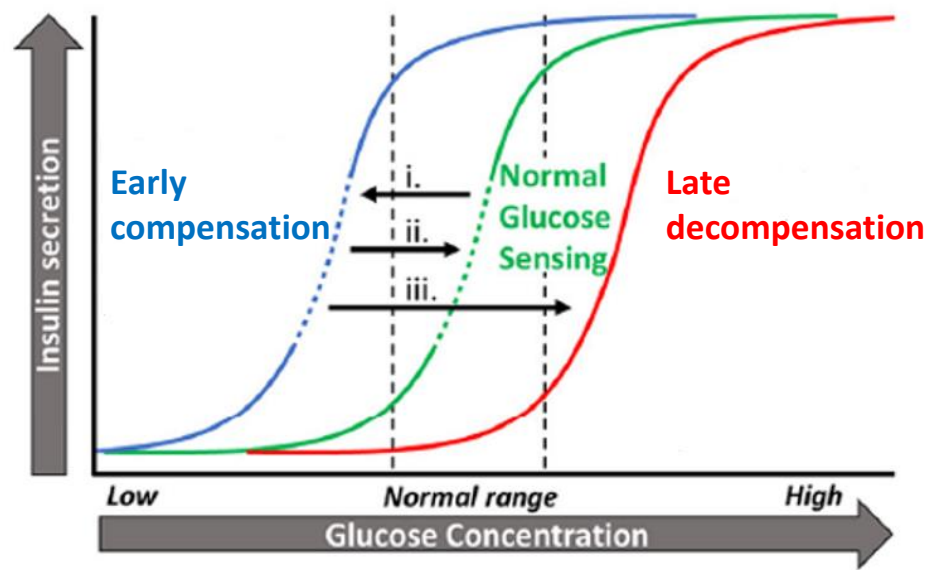
- Older db/db mice, IR/T2D humans
- Right-shifted dose-response curve (relatively or absolutely)
- Hyperglycemia and increased 2h ipGTT
- Insufficiently increased or decreased insulin secretion
- The majority of parameters impaired



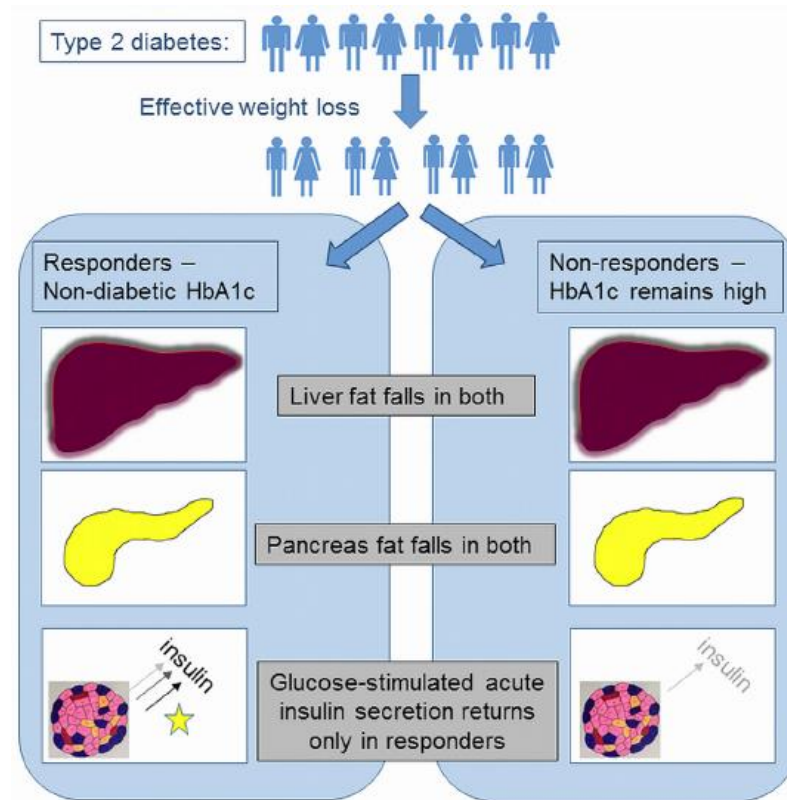
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Etiopatogeneza sladkorne bolezni tipa 2: en korak v levo, dva koraka v desno....



Whitticar & Nunemaker. *Front Endocrinol*; 2020.



Taylor et al. *Cell Metab* ; 2018.



Sladkorna bolezen tipa 2: remisija?

... kratkotrajna kalorična restrikcija ...

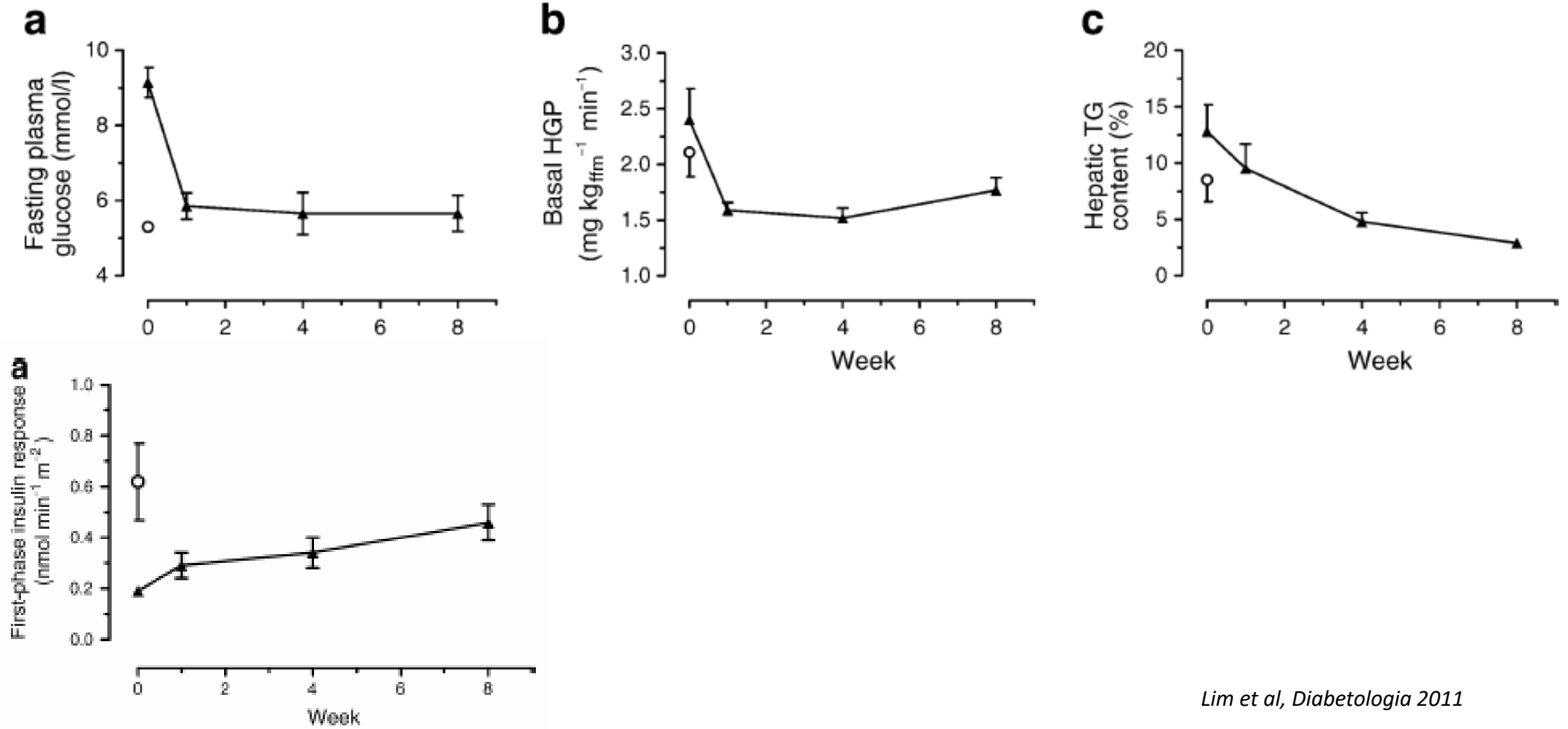


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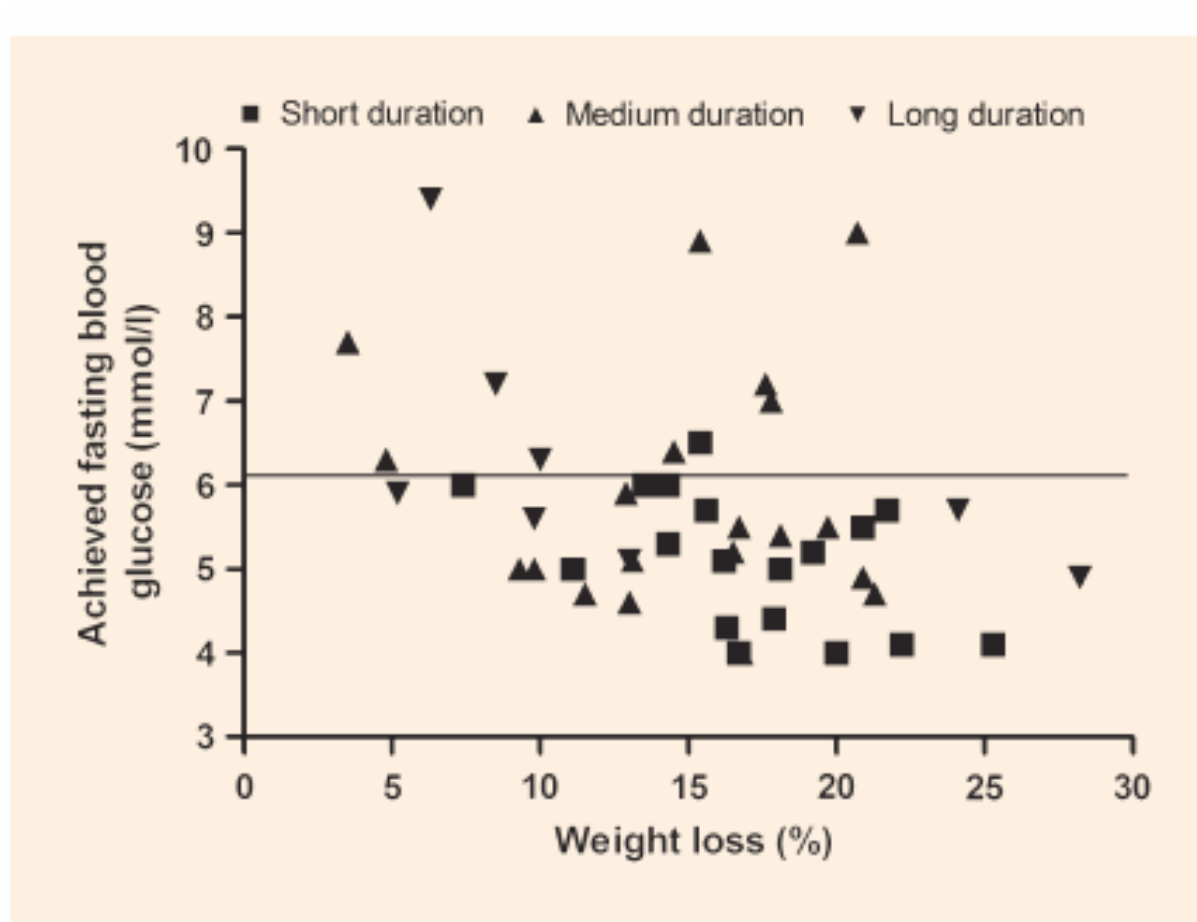
Remisija sladkorne bolezni tipa 2 pri ljudeh

600 kcal/dan, 8 tednov



Lim et al, Diabetologia 2011

Remisija je odvisna od izgube telesne teže



Reversal rates according to diabetes duration:

short (< 4 years) = 73%,
medium (4–8 years) = 56%
long (> 8 years) = 43%.

Steven et al Diab Med 2013



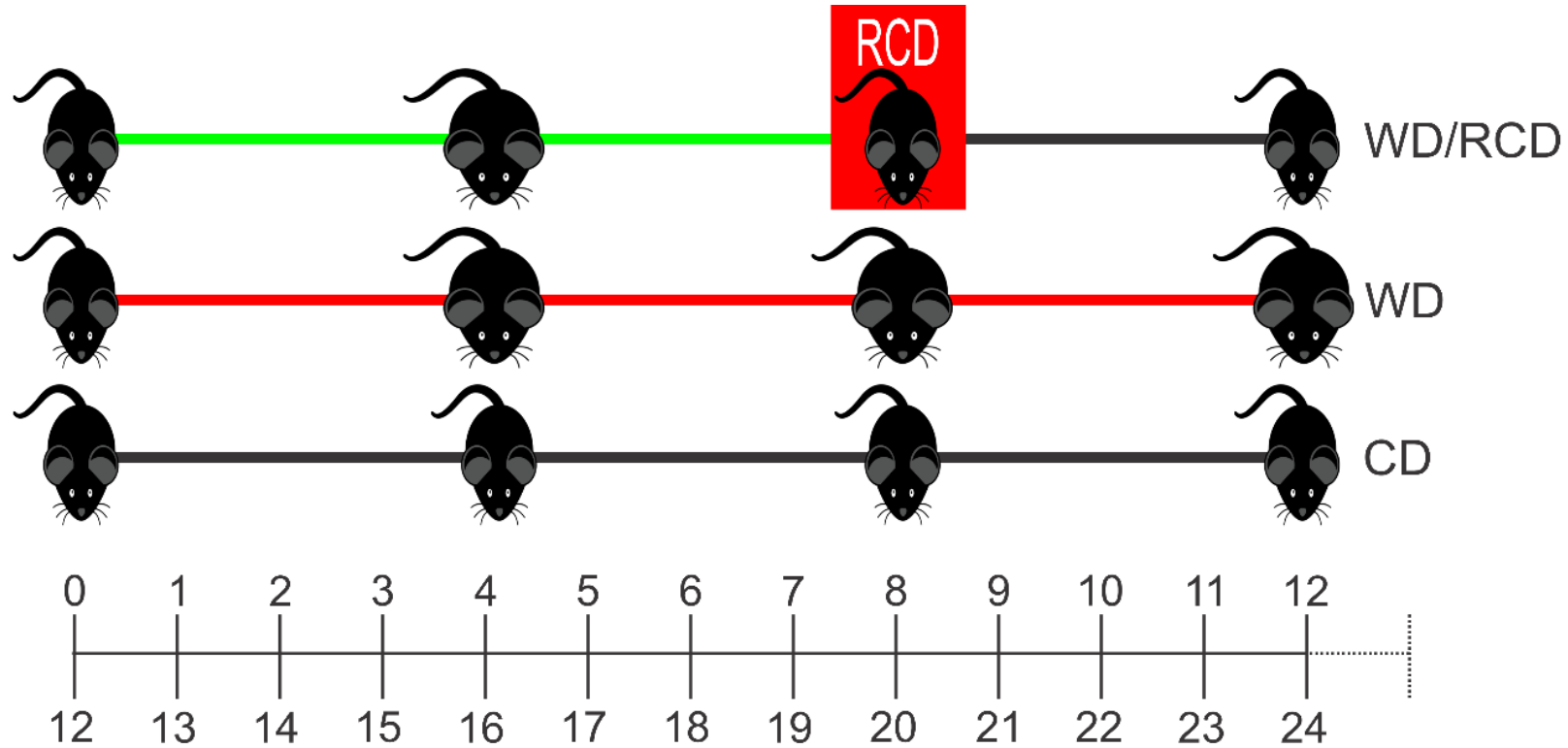
Dolgoročni učinki kalorične restrikcije

Table 1 Sustained benefit on weight and blood glucose levels following a period of energy restriction in eight individuals

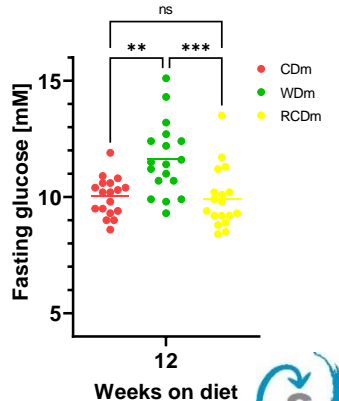
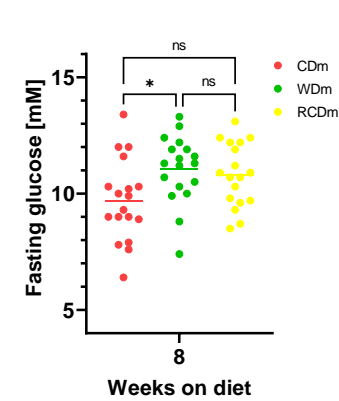
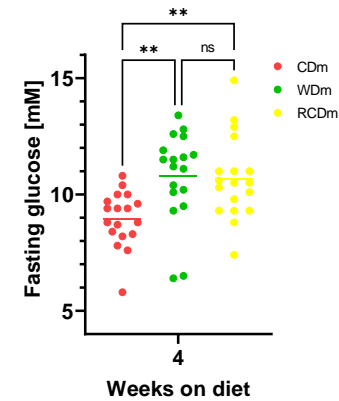
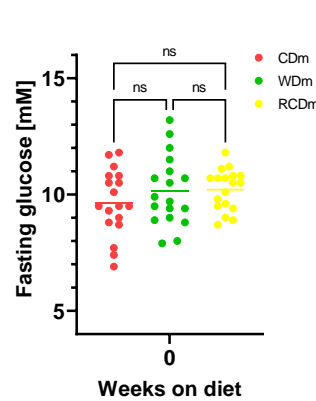
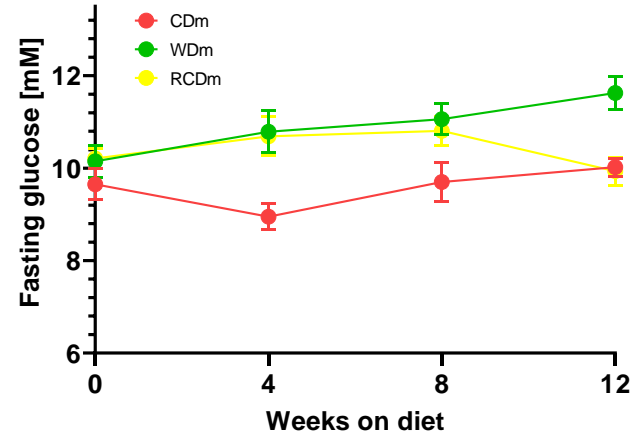
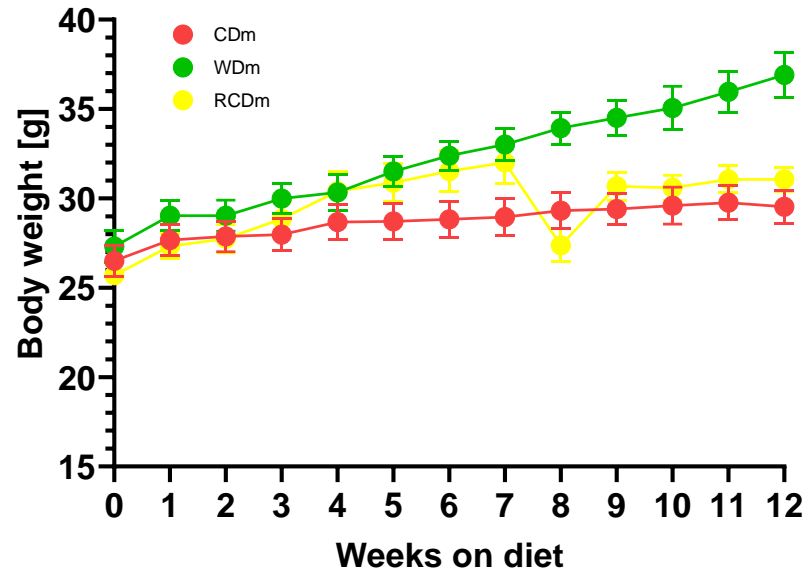
Subject	Time since diet period	Reported glycaemic control at this time	Diabetes duration	Weight Δ during diet (kg)	Weight Δ following diet (kg)
1	8 months	HbA _{1c} 40 mmol/mol (5.8%)	4 months	-7.3	+3
2	7 months	HbA _{1c} 36 mmol/mol (5.4%)	3 years	-30.4	-12.4
3	5 months	HbA _{1c} 35 mmol/mol (5.4%)	1 year	-18	+5
4	5 months	HbA _{1c} 39 mmol/mol (5.7%)	3 years	-20.4	+2.2
5	5 months	HbA _{1c} 33 mmol/mol (5.2%)	6 months	-17	+7.5
6	5 months	HbA _{1c} 38 mmol/mol (5.6%)	8 months	-25.4	+5.4
7	3 months	Oral glucose tolerance test Fasting plasma glucose 6.1 mmol/l 2-h plasma glucose 6.3 mmol/l	4 years	-17.5	+2.5
8	3 months	Oral glucose tolerance test Fasting plasma glucose 5.1 mmol/l 2-h plasma glucose 6.0 mmol/l	6 months	-18	-3



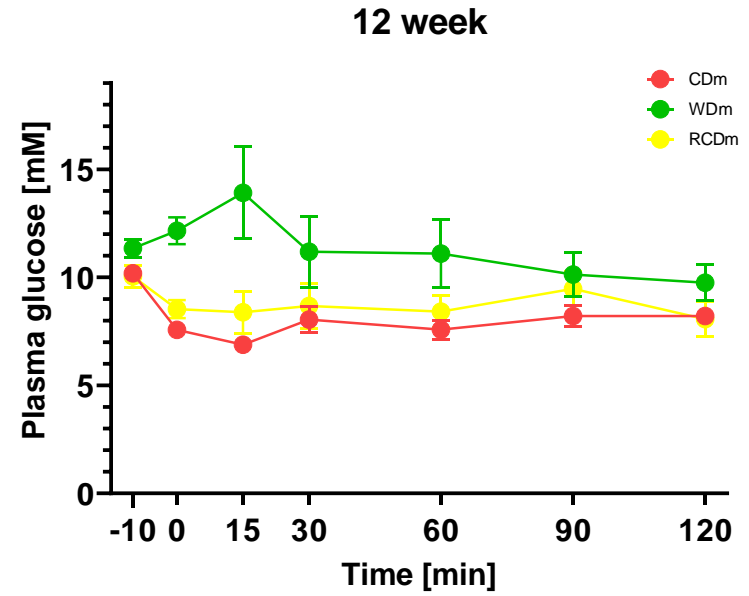
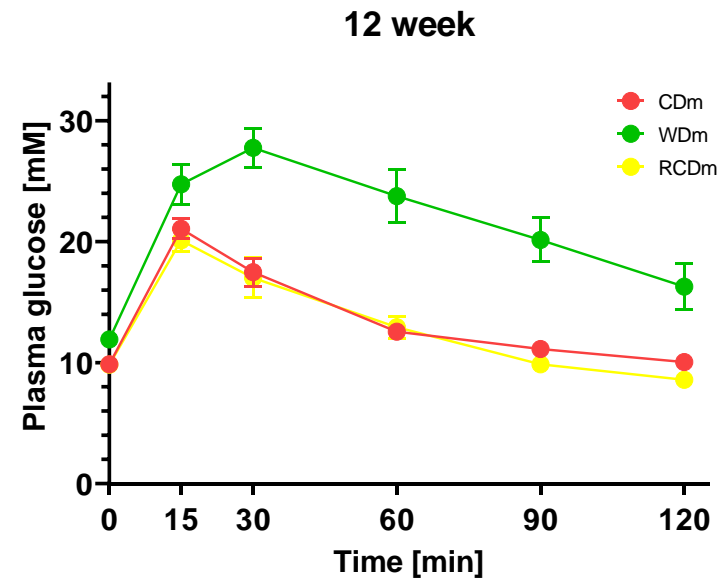
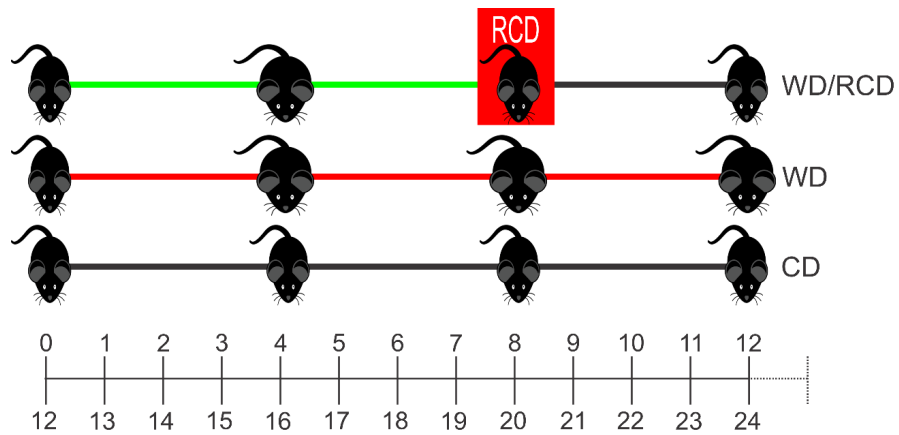
Mišji model – orodje raziskovanja



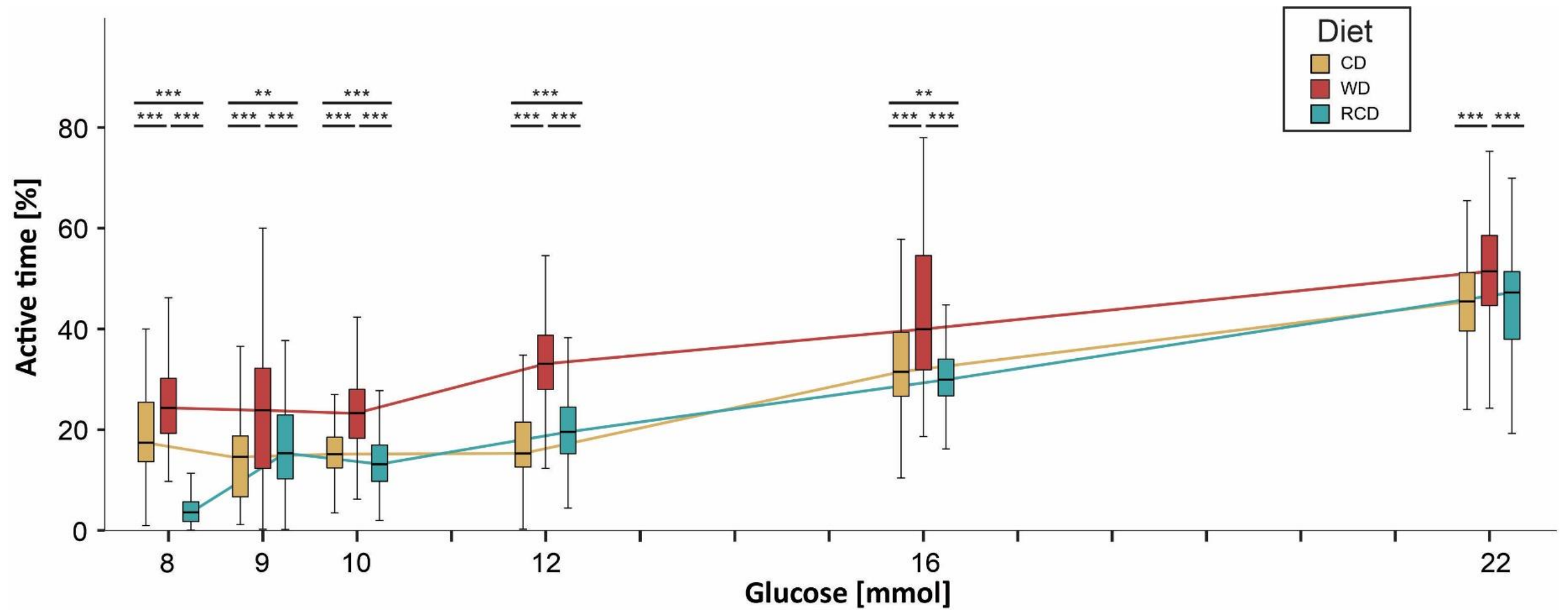
Mišji model – orodje raziskovanja



Mišji model – orodje raziskovanja



Mišji model – orodje raziskovanja



* $P < 0.05$

** $P < 0.01$

*** $P < 0.001$

**** $P < 0.0001$

Povzetek

- Mišji modeli sladkorne bolezni pomagajo razumeti razvoj sladkorne bolezni tipa 2 in predstavljajo platformo za razvoj novih (ne)farmakoloških pristopov.
- Spremembe v funkciji endokrinih celic: „en korak v levo, dva koraka v desno“.
- Intermitentna kalorična restrikcija omogoči remisijo zgodnje sladkorne bolezni tipa 2.





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