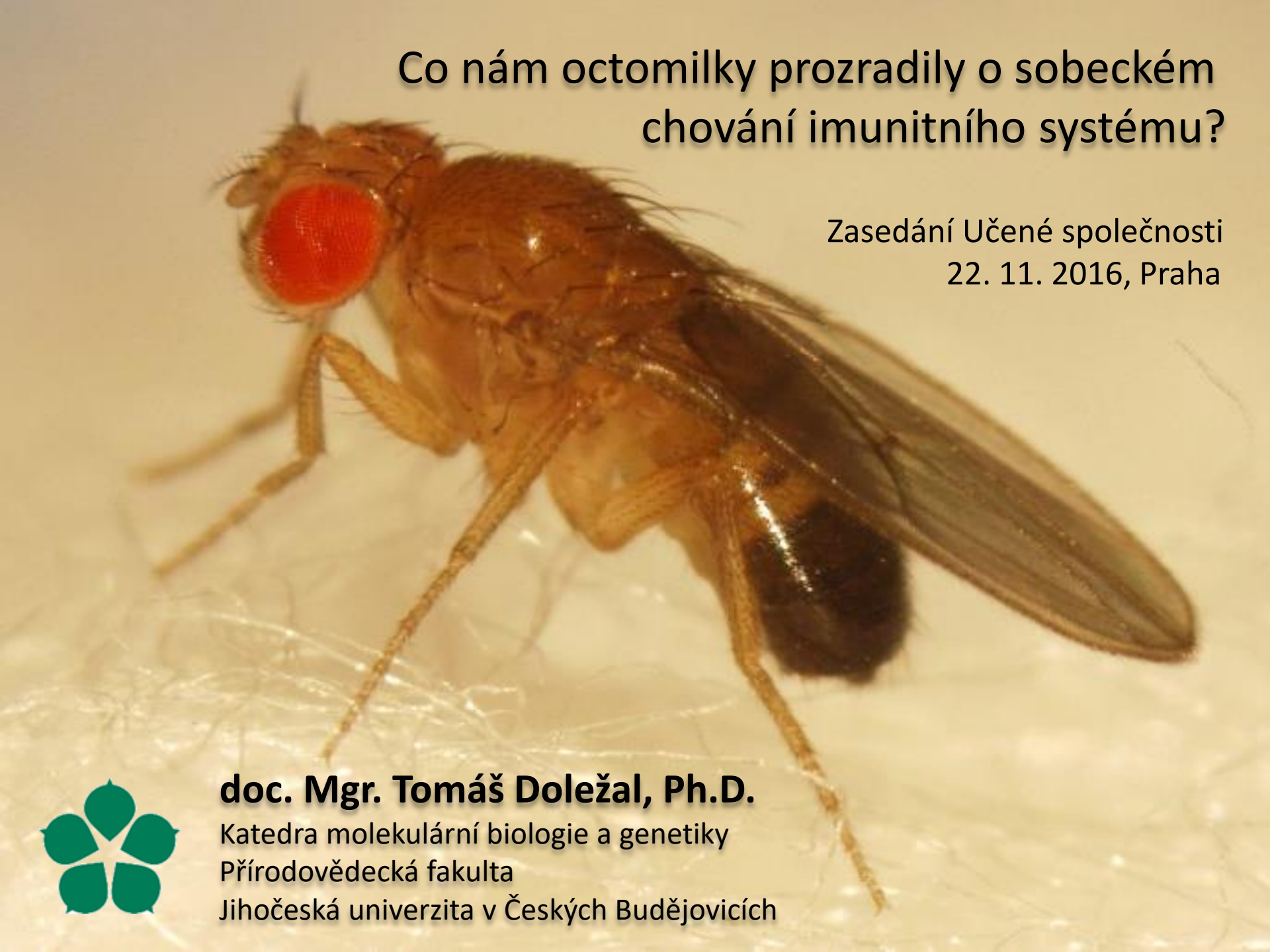
Co nám octomilky prozradily o sobeckém chování imunitního systému?

Zasedání Učené společnosti
22. 11. 2016, Praha



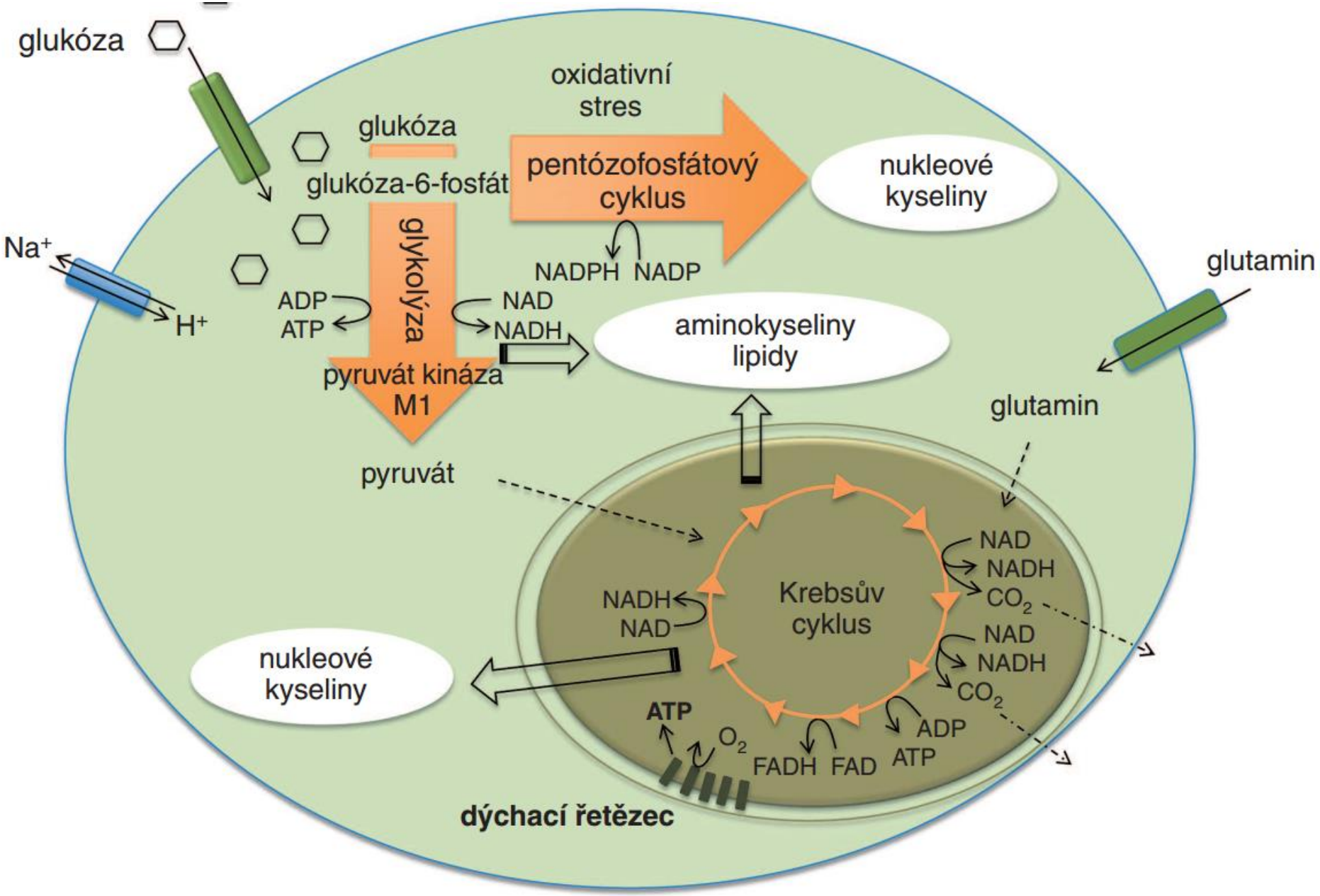
doc. Mgr. Tomáš Doležal, Ph.D.
Katedra molekulární biologie a genetiky
Přírodovědecká fakulta
Jihočeská univerzita v Českých Budějovicích

Když jsme nemocní, chybí nám „energie“ …

Systém/orgán	**Spotřeba energie za den (kJ/day)**
Celkový bazální metabolizmus	7,000
Celkový metabolizmus při běžné aktivitě	**10,000**
Celkový metabolizmus při sepsi	**15,000**
Imunitní systém za normálních podmínek	**1,600**
Imunitní systém při střední aktivaci	**2,100**

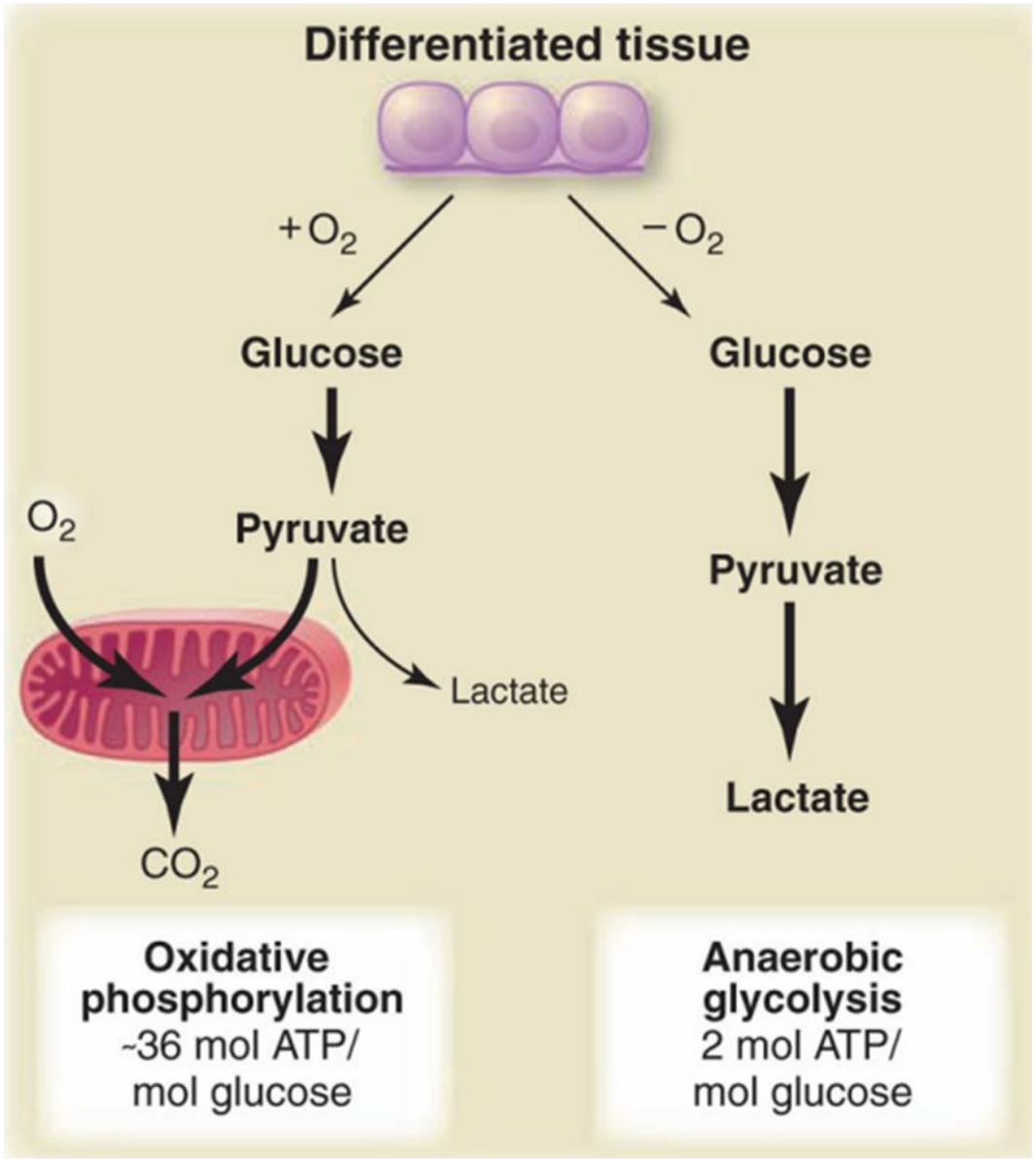
Proč dochází ke zvýšení spotřeby energie při aktivaci imunitního systému?

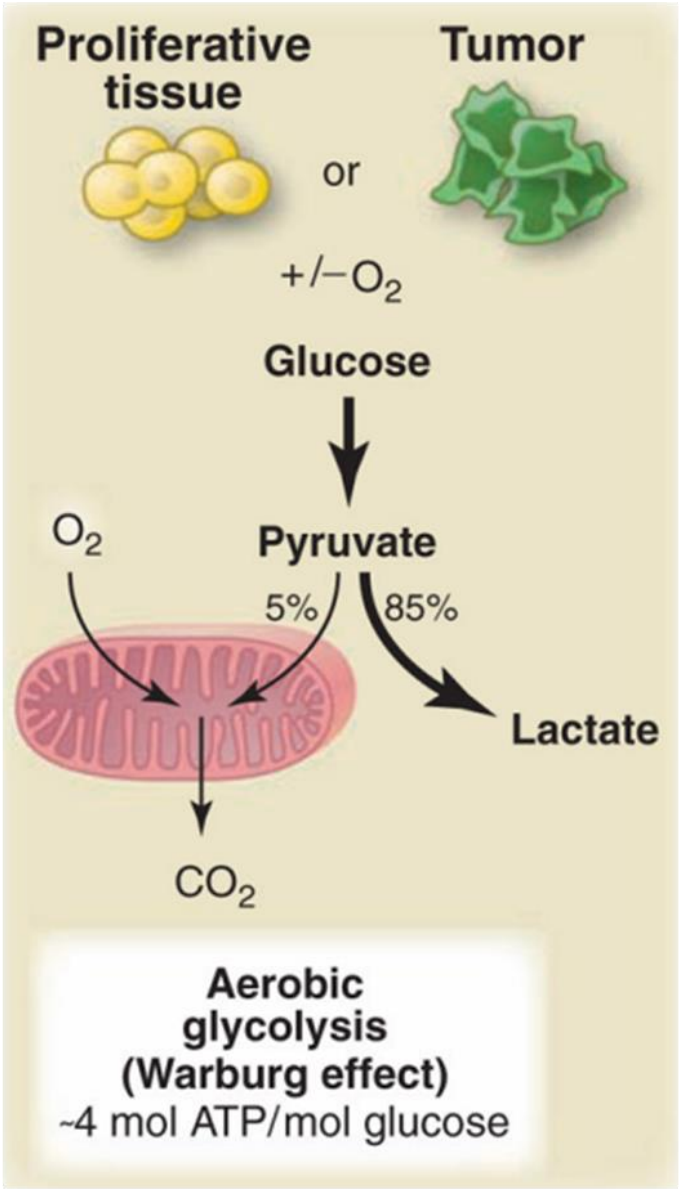
Spies *Arthritis research & therapy* 2012



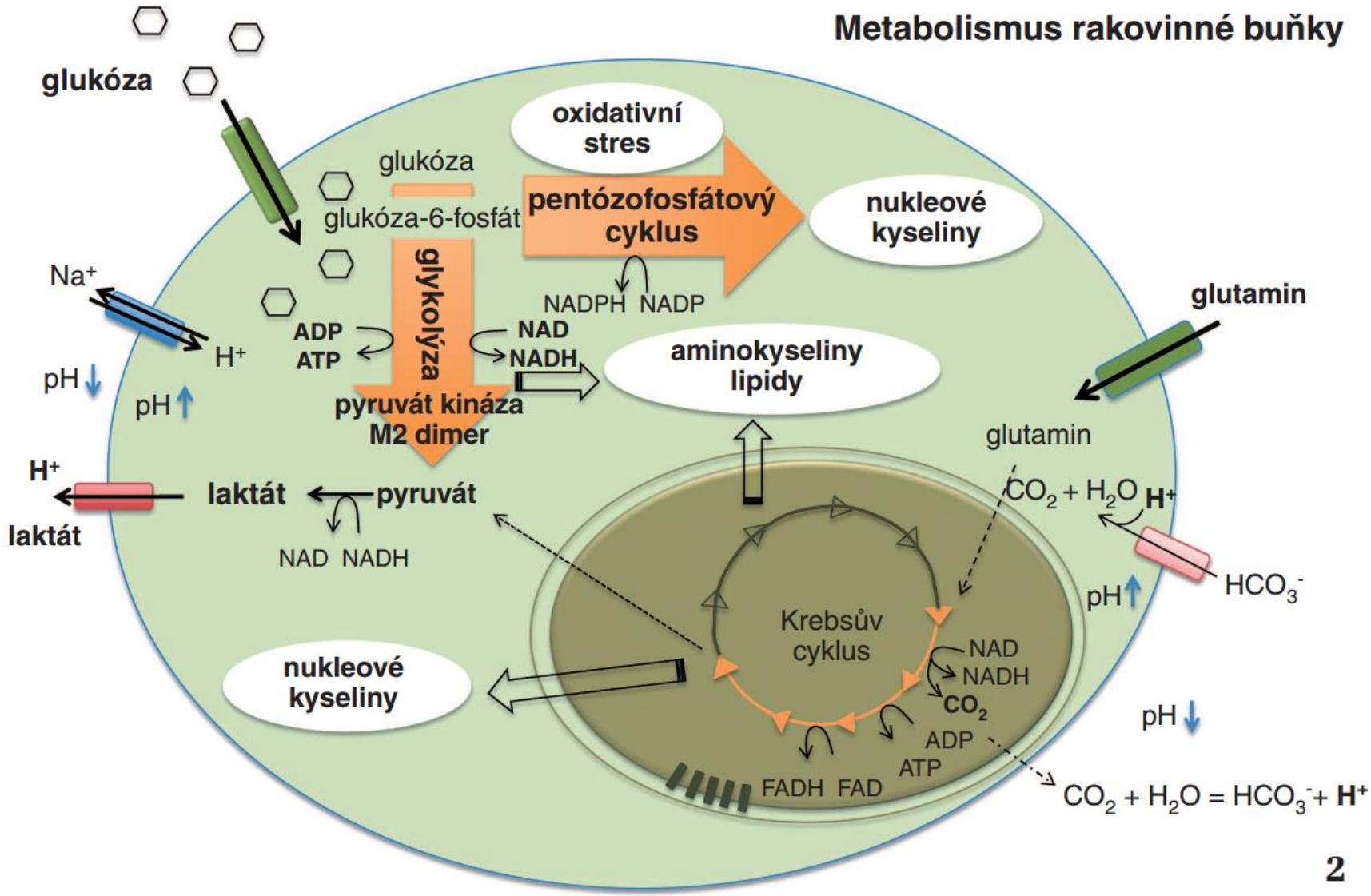
Slaninová a Krejčí, Živa 2013

Warburg efekt – zvýšená glykolýza i za přísunu kyslíku



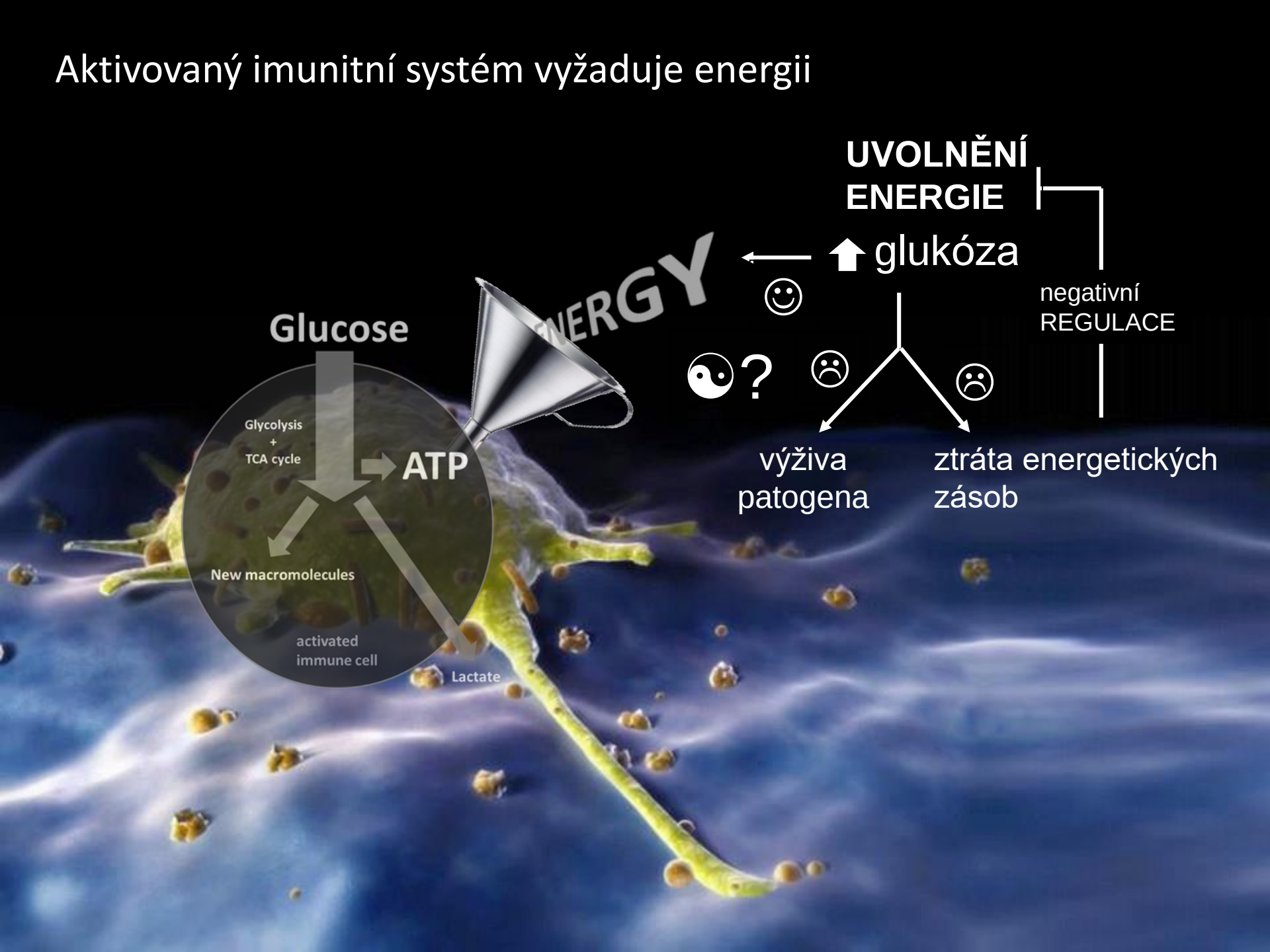


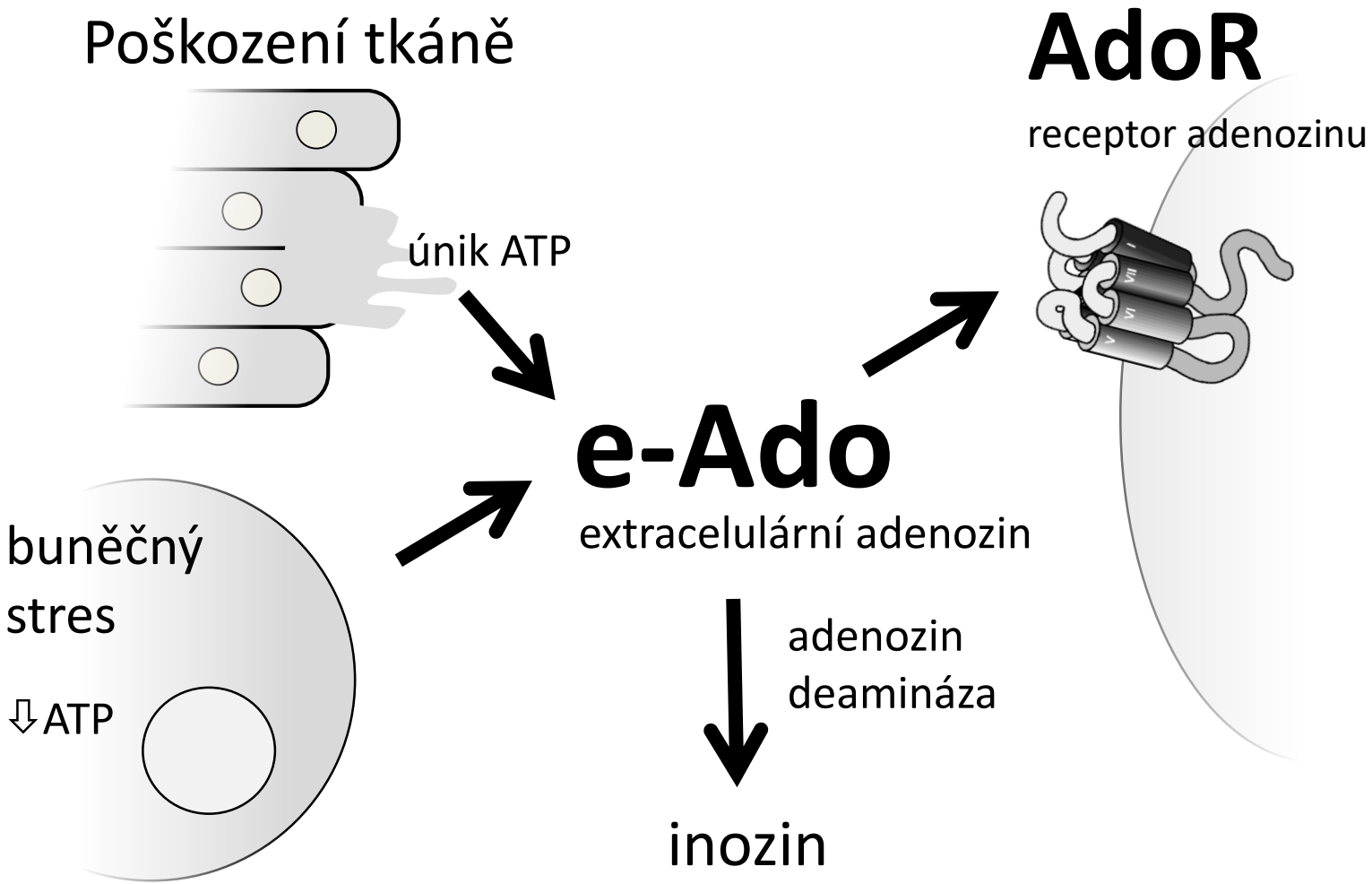
Vander Heiden *Science* 2009



Slaninová a Krejčí, Živa 2013

Aktivovaný imunitní systém vyžaduje energii



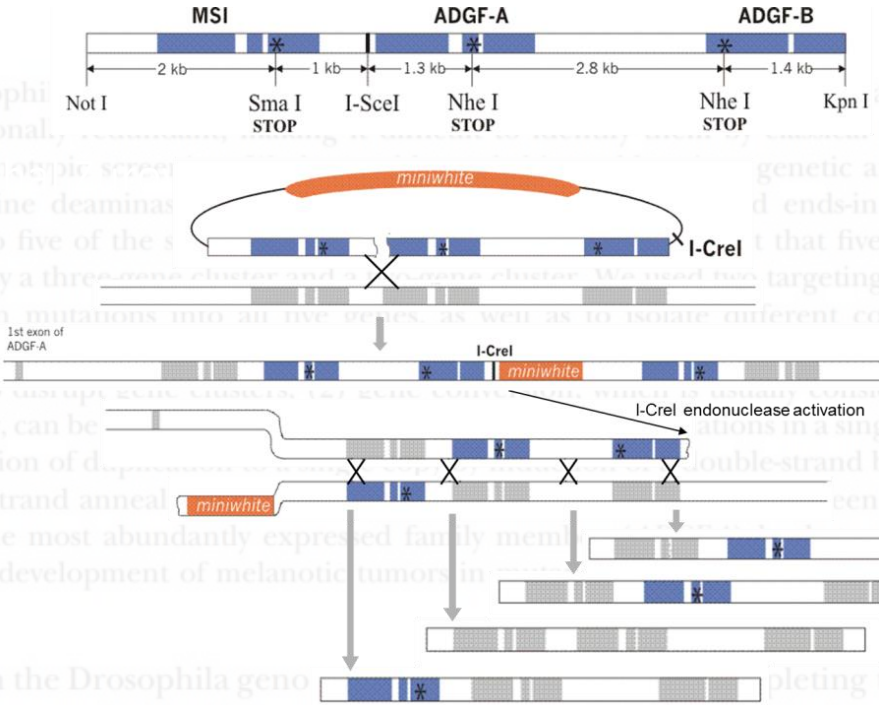

Poškození tkáně
únik ATP
buněčný stres
⇩ATP
e-Ado
extracelulární adenozin
adenozin deamináza
inozin
AdoR
receptor adenozinu

Genetic Analysis of the *ADGF* Multigene Family by Homologous Recombination and Gene Conversion in Drosophila

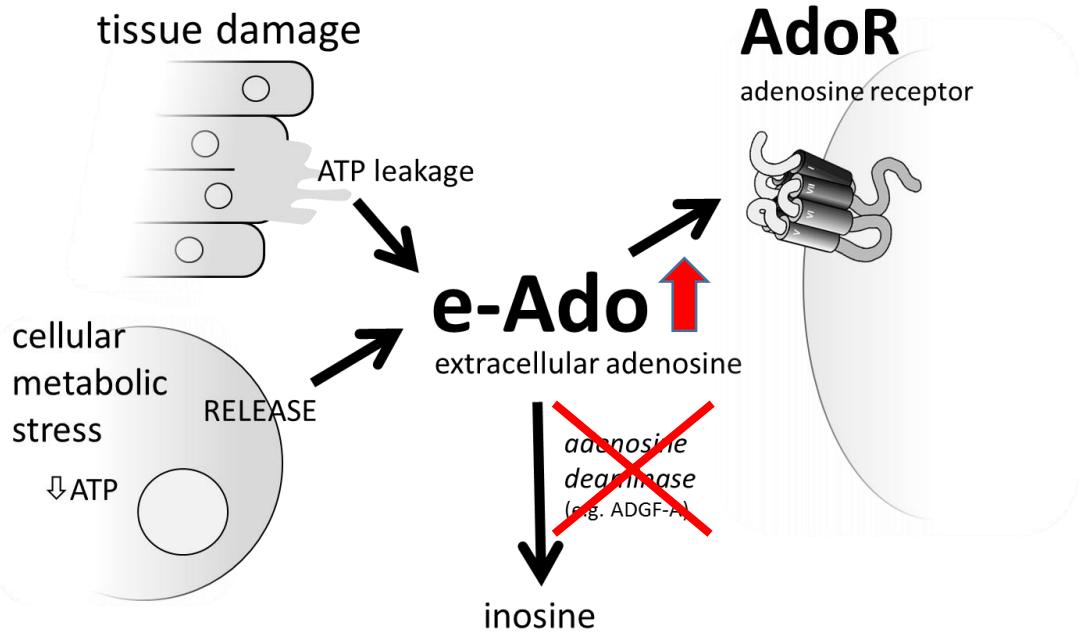
Tomas Dolezal,*,†,1 Michal Gazi,*,†,1 Michal Zurovec*,† and Peter J. Bryant*,2

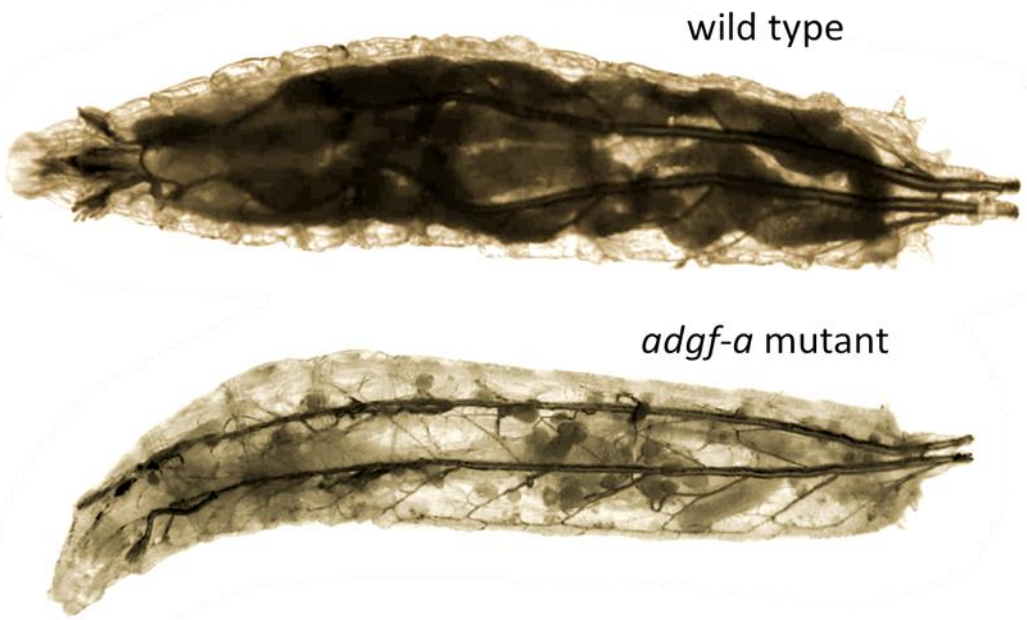
*Developmental Biology Center, University of California, Irvine, California 92697 and †Institute of Entomology and University of South Bohemia, 37005 Ceske Budejovice, Czech Republic

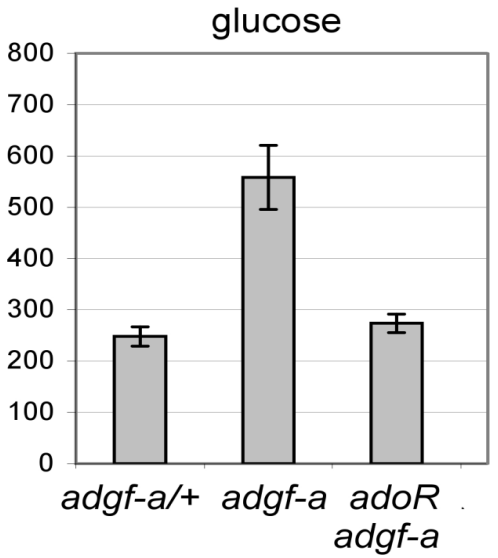
Manuscript received March 11, 2003
Accepted for publication June 2, 2003



Dolezal et al. 2003 – *Genetics*

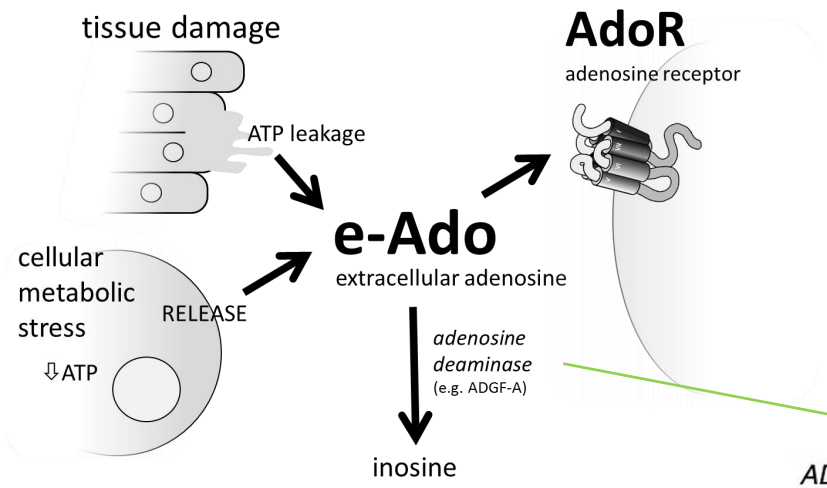






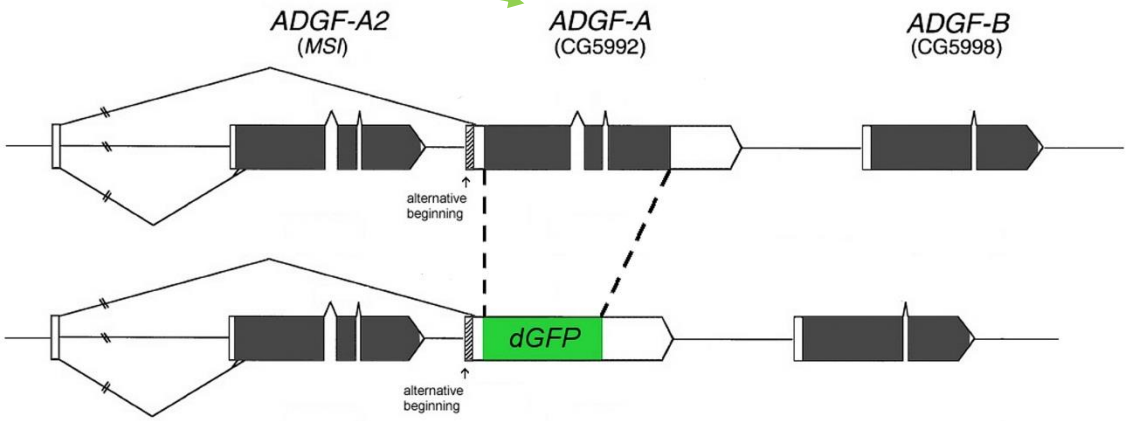
Dolezal et al. 2005 – *Plos Biology*

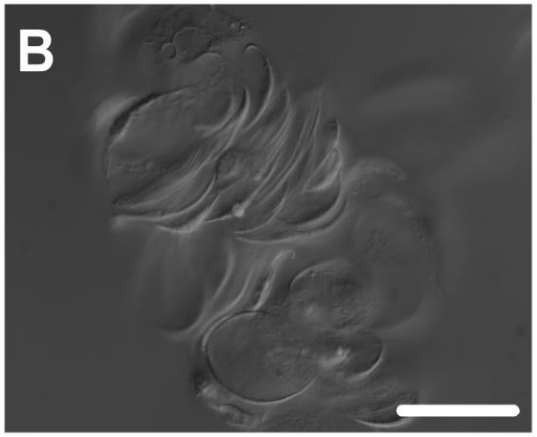
Zuberova, et al. 2010 - *Dis Model Mech*

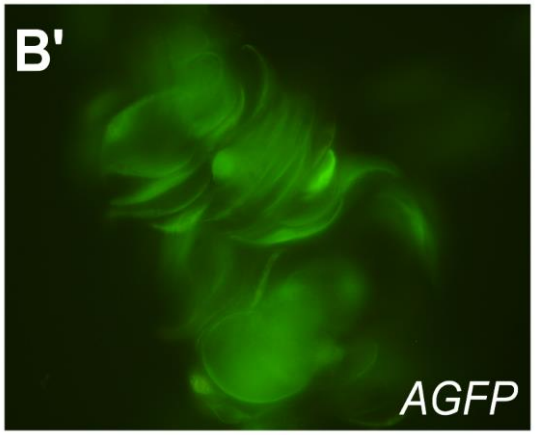


ADGF-A expresní reportér

pomocí homologní rekombinace





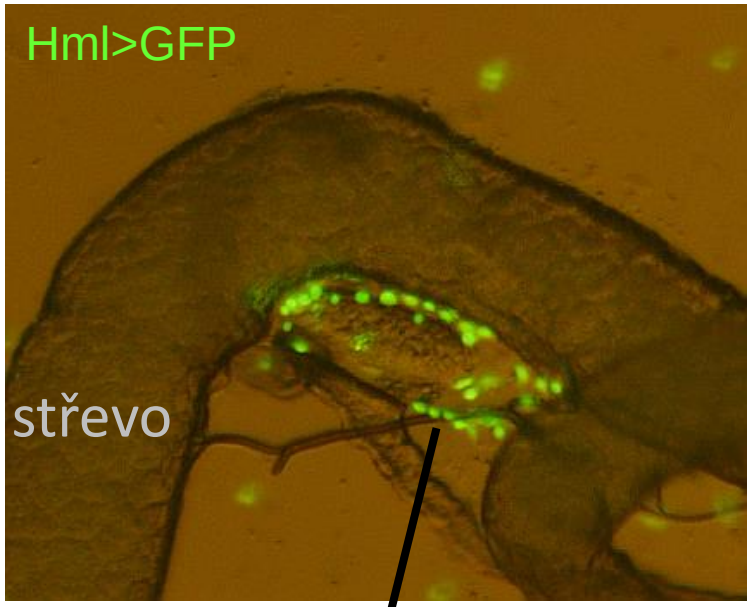


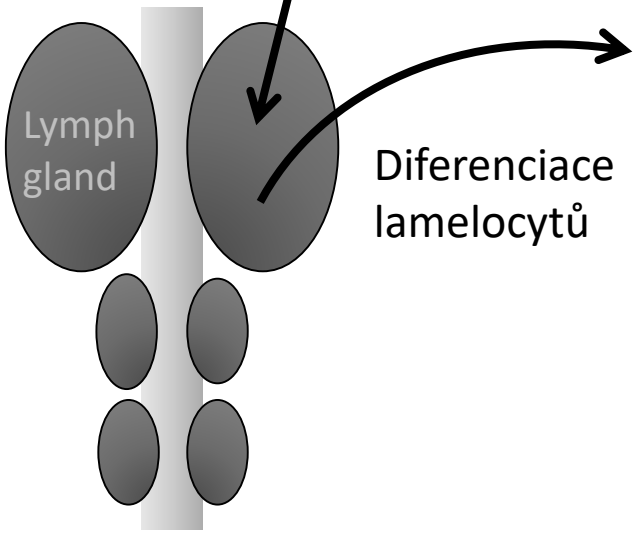
lamelocyty

(Novakova and Dolezal, PLoS One 2011)


Parazitoidní vosička
Leptopilina boulardi
larva
Drosophila melanogaster

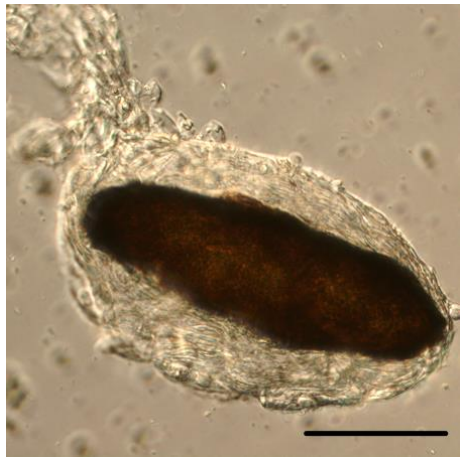
Rozeznání vajíčka



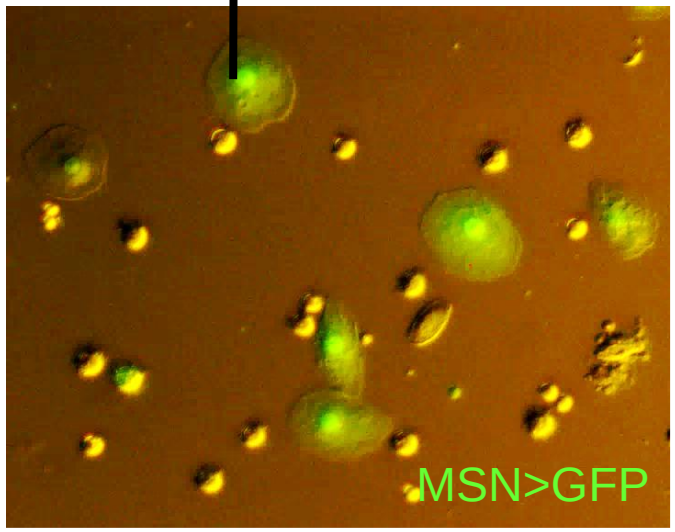


Diferenciace lamelocytů

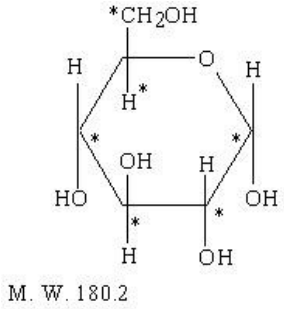
Enkapsulace vajíčka a melanizace



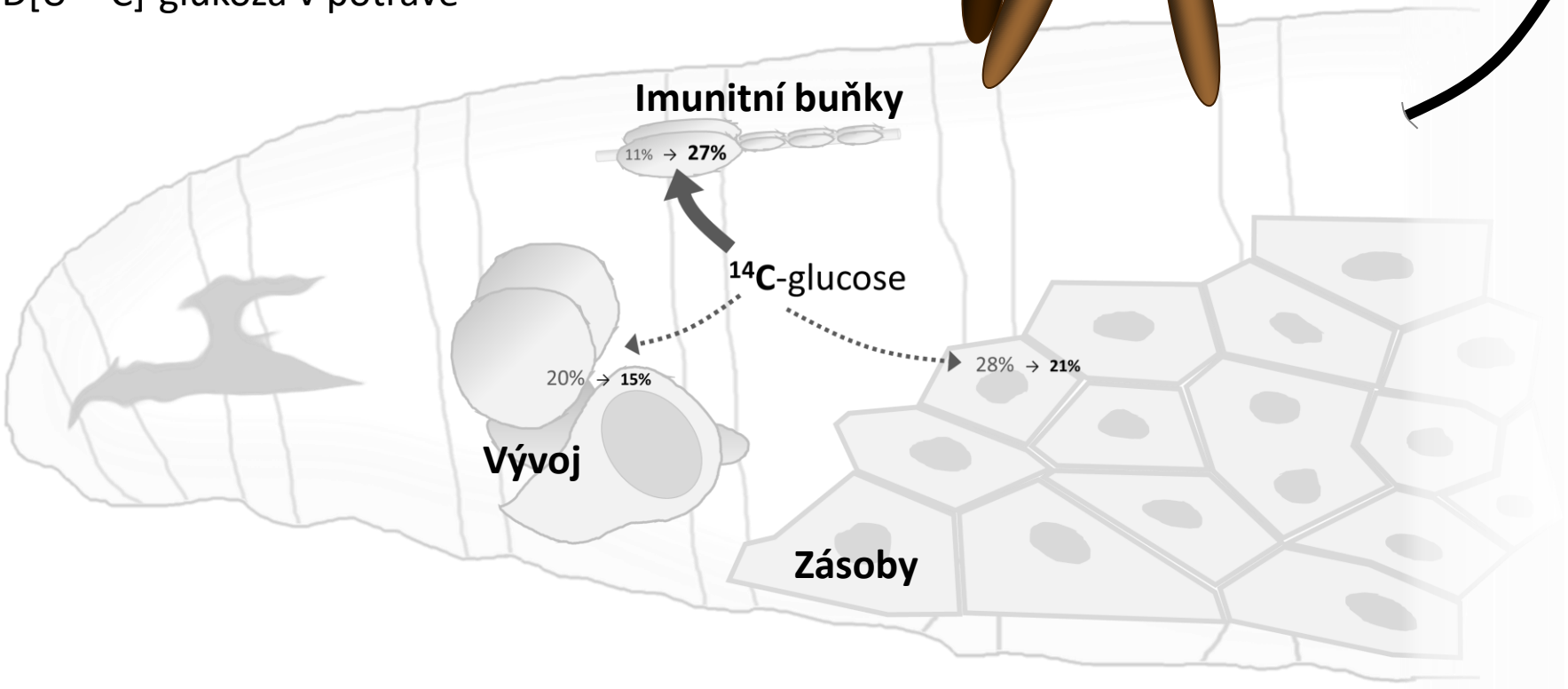
během 48 hodin



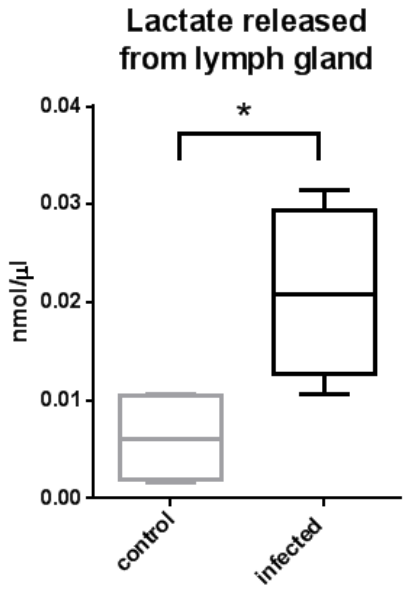
během 24 hodin



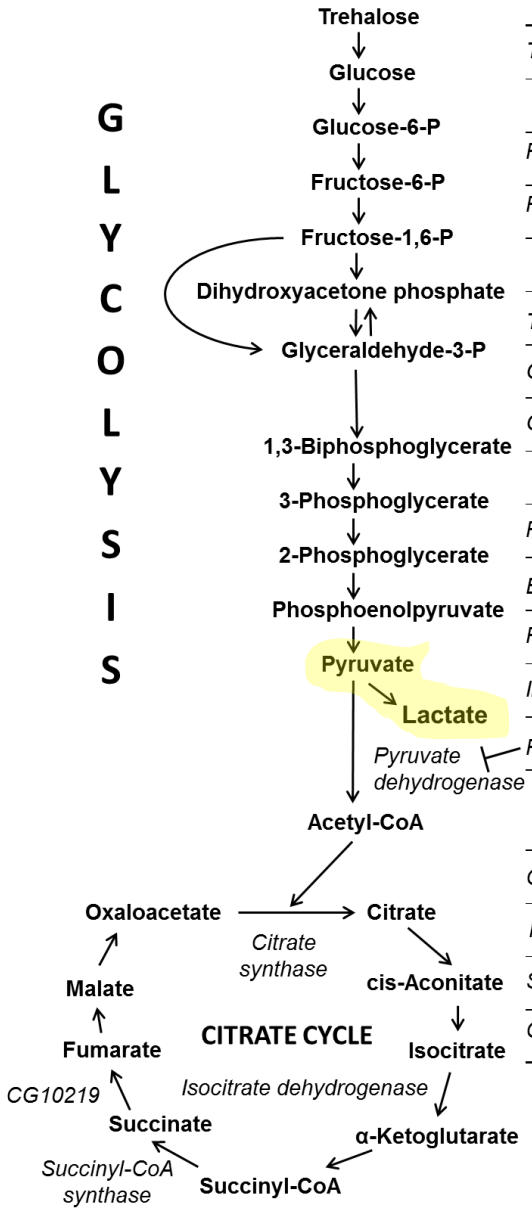
D[U-^{14}C]-glukóza v potravě



Imunitní buňky mouchy zvyšují glykolýzu (Warburg)

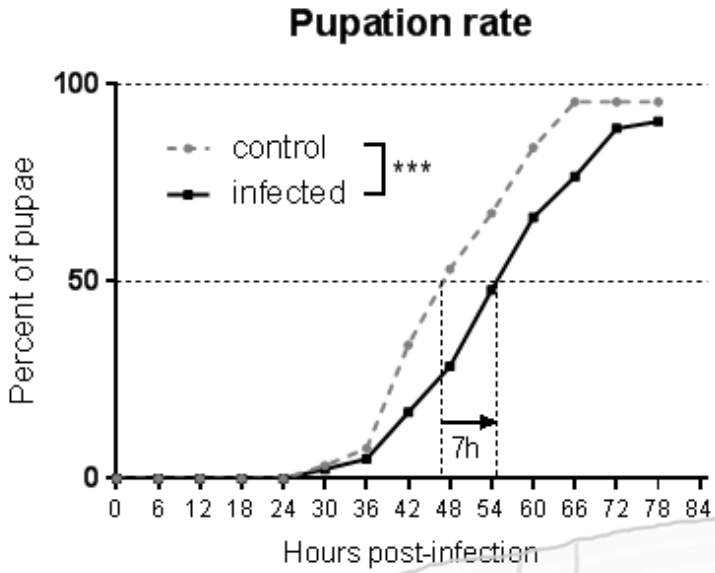


(Strasser and Dolezal, unpublished)

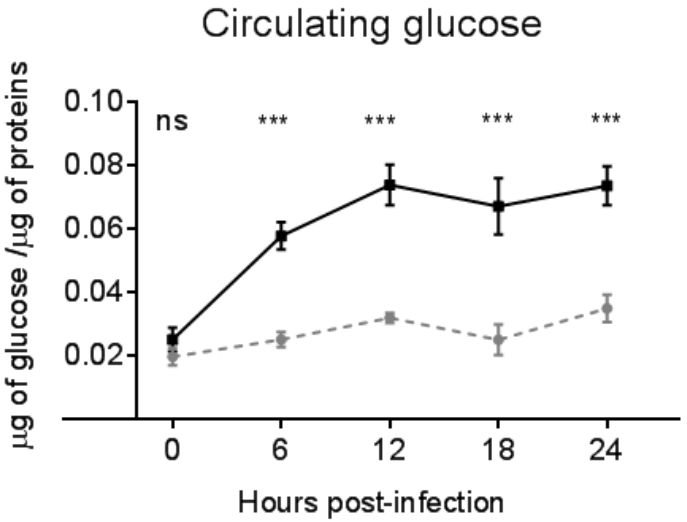


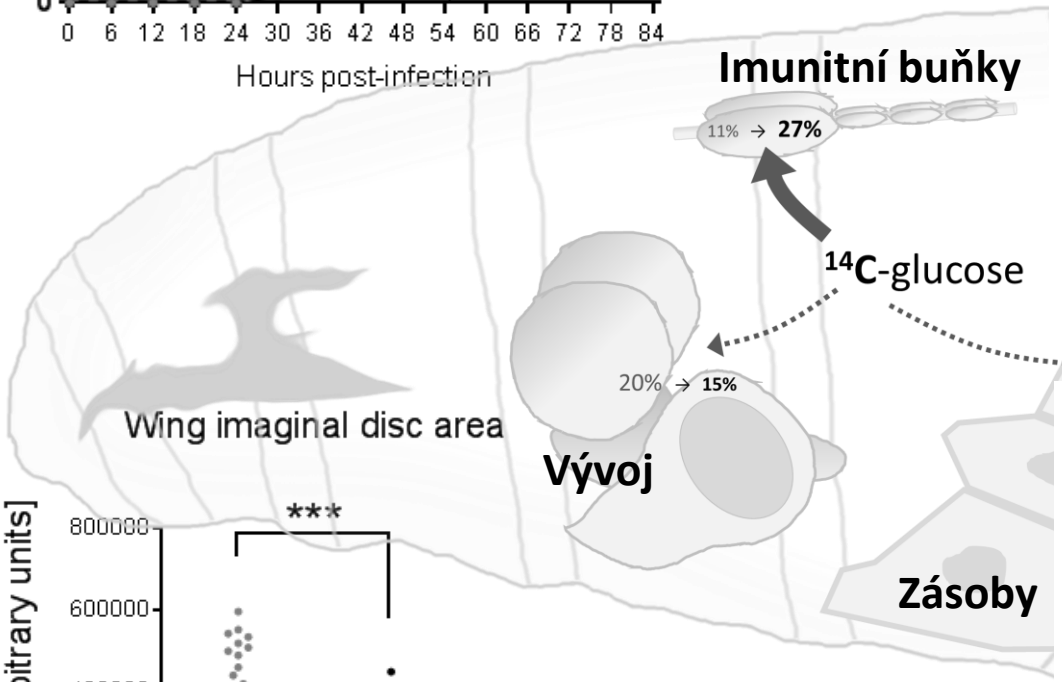
tissue	Hemo-cytes		Lymph gland		Fat body	
hours postinfection	6	18	6	18	6	18
Trehalase						
Phospho-glucose isomerase						
Phospho-fructose kinase						
Triose-phosphate isomerase						
Gapdh1						
Gapdh2						
Pglym78						
Enolase						
Pyruvate kinase						
Impl3						
Pdk						
Citrate synthase						
Isocitrate dehydrogenase						
Succinyl-CoA synthase						
CG10219						

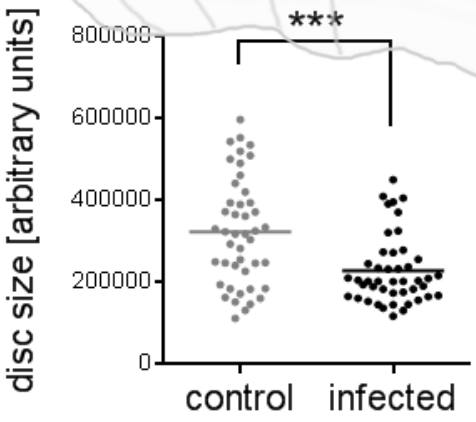
no change
increased expression
decreased expression

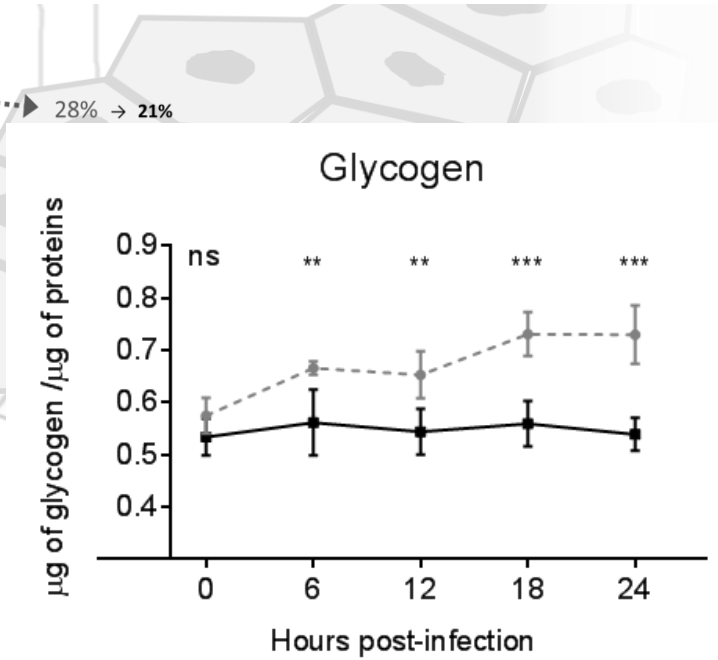


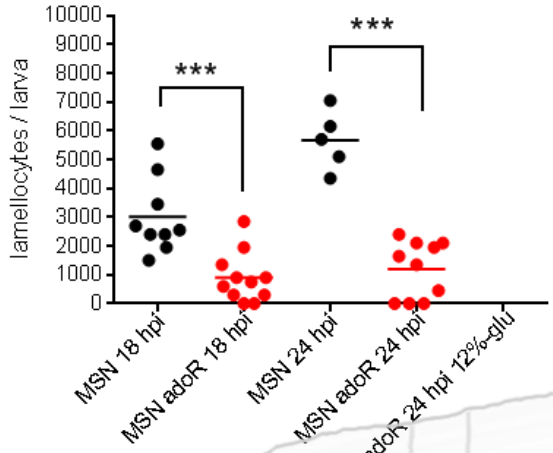
spíše vývoj nebo imunita?

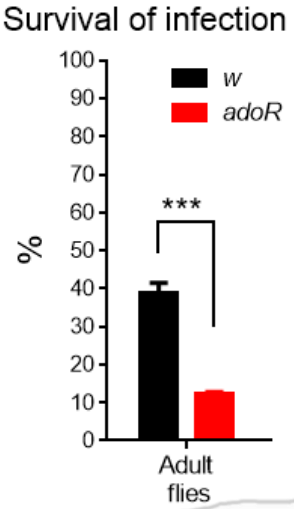


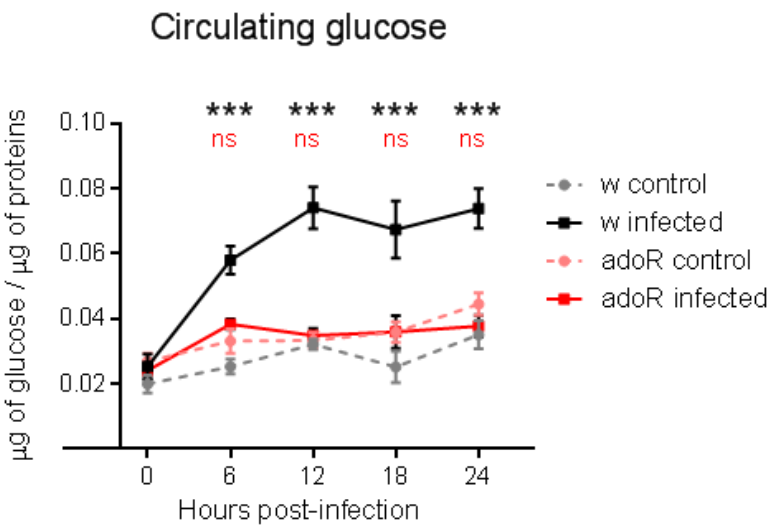


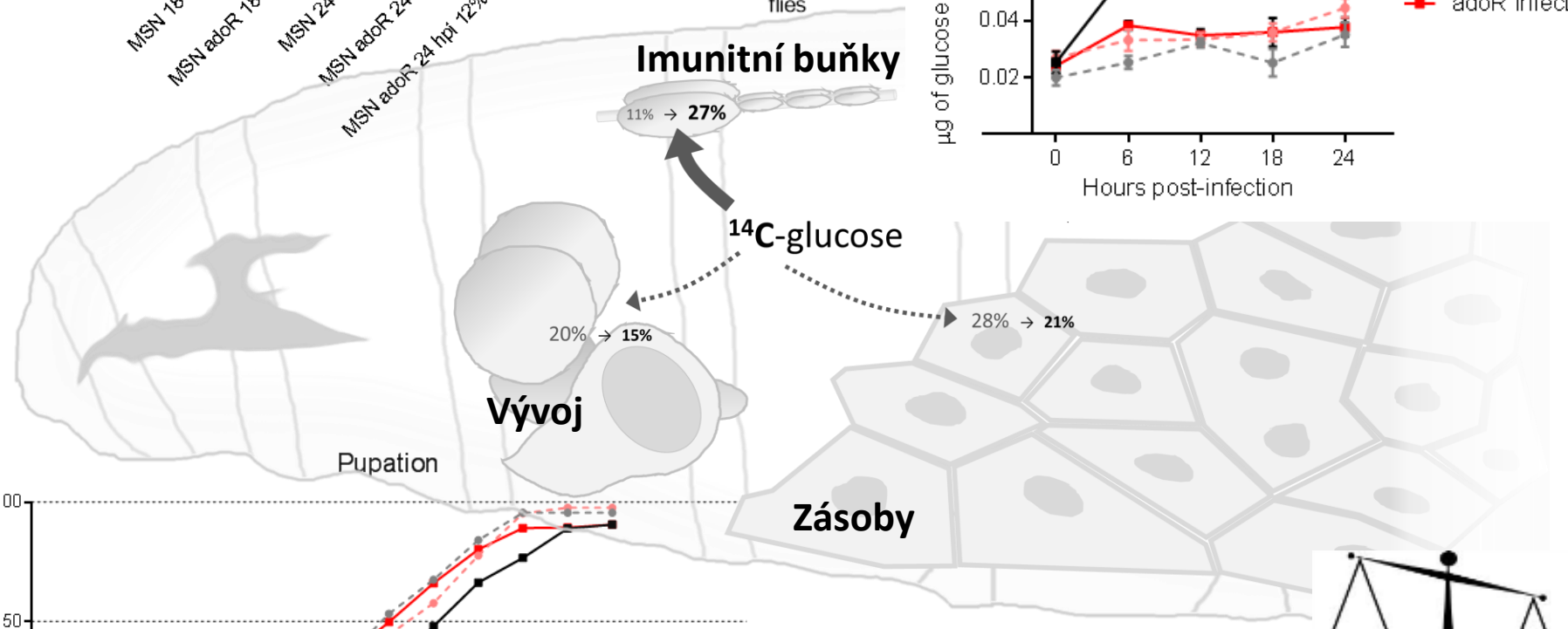


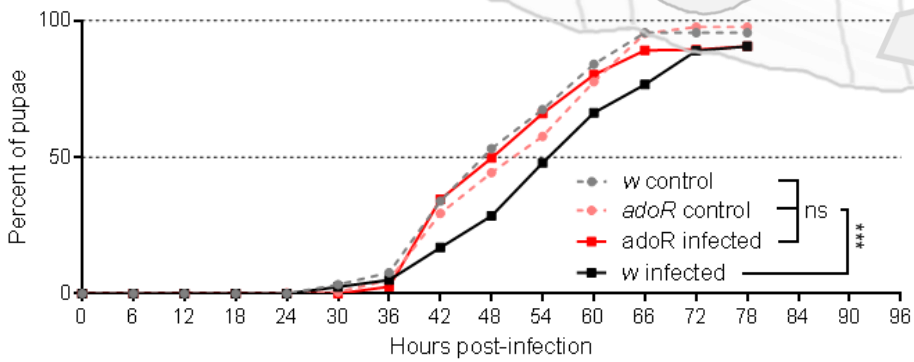




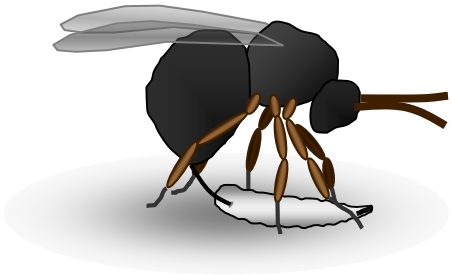








Experimentální ověření



rozeznání vajíčka

enkapsulace

parasitoid

aktivace

pro-hemocyt
↑ aerobní glykolýza

proliferace

diferenciace

lamelocyt

vyvíjející se larvální tkáň

e-Ado

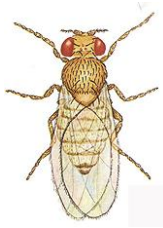
AdoR

GLUKÓZA

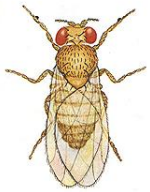
UAS-Gal4 systém

Bloomington, Indiana

různé tkáně:
tukové těleso
imunitní buňky …



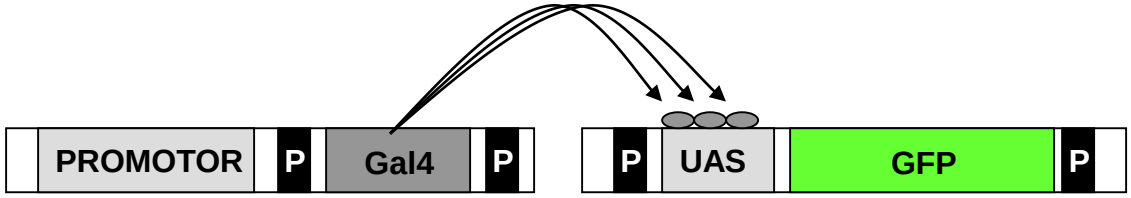
promotor - Gal4



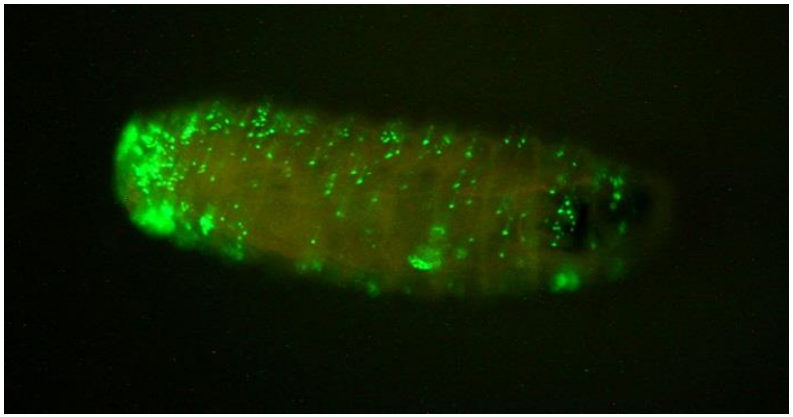
UAS – kódující sekvence

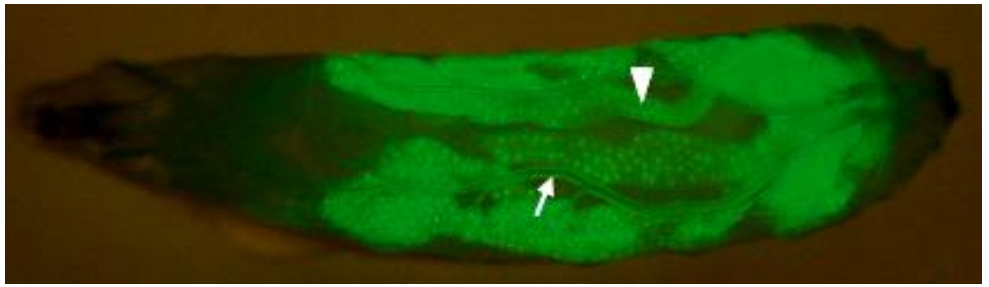
Vídeň- Nukleosidový transportér

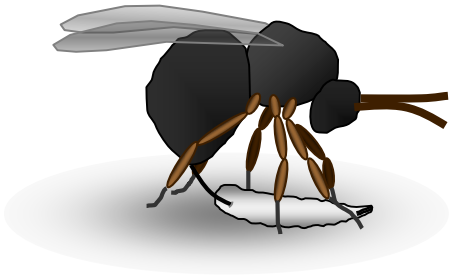
RNA interference = umlčení genu



potomek







rozeznání vajíčka

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vyvíjející se larvální tkáň

e-Ado

AdoR

GLUKÓZA

SOBECKÝ IMUNITNÍ SYSTÉM

April 27, 2015

Adenosine Secures Energy for Immune Activity

A study of the fruit fly's response to parasitoid wasp eggs by Adam Bajgar, Tomas Dolezal and co-workers reveals that immune cells selfishly release adenosine as a signal to trigger a systemic metabolic switch, thereby suppressing non-immune processes and securing energy and nutrients for immune activity. Read the Primer by Brian Lazzaro.

Image credit: Tomas Dolezal

FORMAL COMMENTS 04/24/2015

Inclusive Fitness Debate Continues

In a Formal Comment, Martin Nowak and Benjamin Allen challenge the claims of a recent theoretical study by David Queller and colleagues about the role of genetic relatedness in the evolution of eusociality. Queller and co reply.

Image credit: Flickr user Thinkpanther

RECENTLY PUBLISHED ARTICLES

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CURRENT ISSUE

March 2015

Straub *Arthritis Research & Therapy* 2014, **16(Suppl 2)**:S4
http://arthritis-research.com/content/16/S2/S4

arthritis research&therapy

REVIEW

Insulin resistance, selfish brain, and selfish immune system: an evolutionarily positively selected program used in chronic inflammatory diseases

Rainer H Straub*

Email from Rainer Straub: *"Now, I had the chance to read your paper: I was very much impressed by the perfect and extensive work. It is fantastic because it exactly confirms the theory …"*

Sobecký imunitní systém
akutně ☺
chronicky ☹

Systemický přesmyk metabolismu

Insulin

Inzulinová rezistence

glucose

InR

IRS

trans-location

glucose

GluT

PI3K/Akt

JNK

glycolysis

FOXO

FOXO

growth

e.g. muscle cell

Sobecký signál
(TNF-α, IFN-γ, IL-6)

Glucose

WARBURG

Glycolysis + TCA cycle

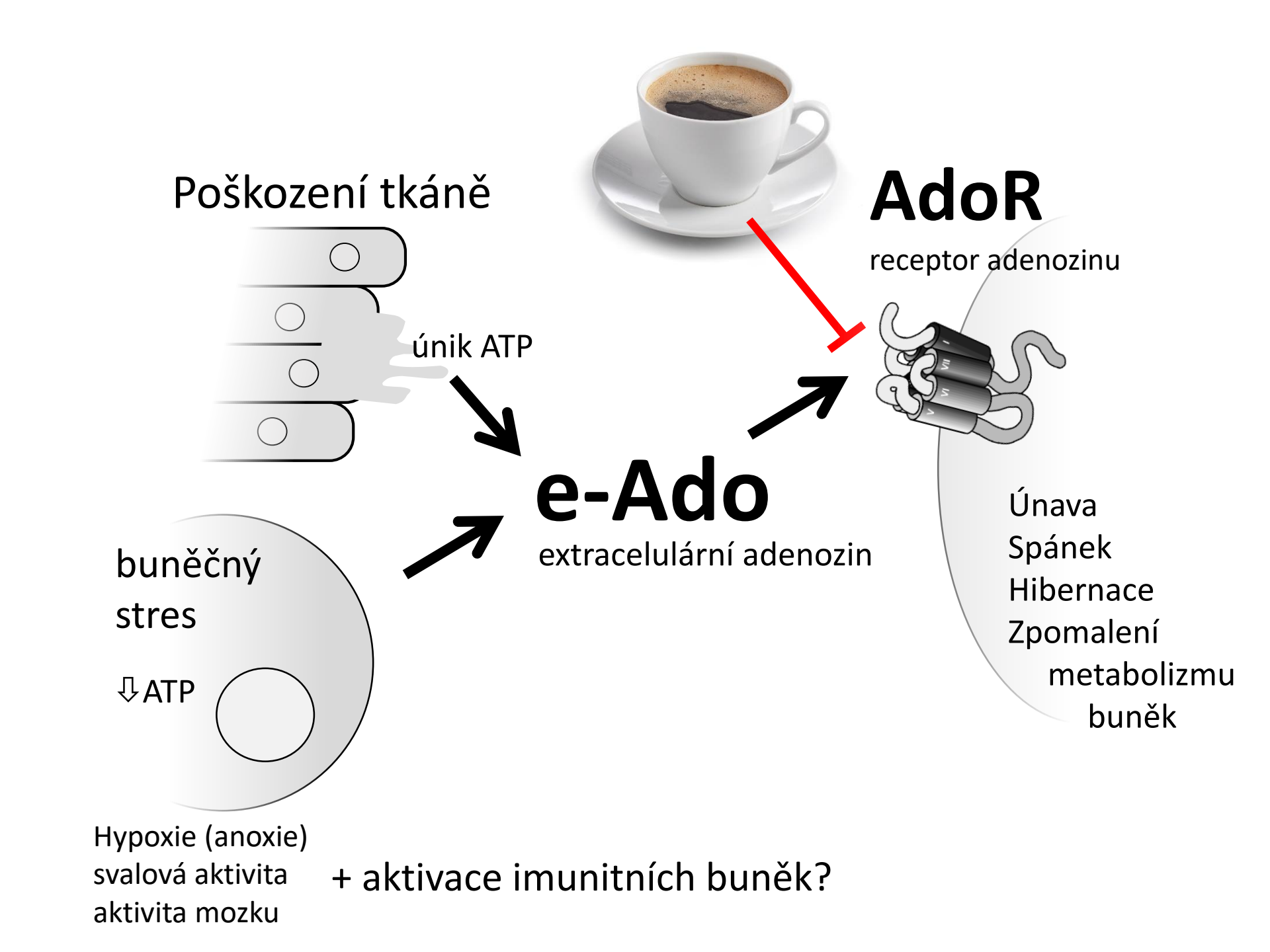
ATP

e-Ado

New macromolecules

activated immune cell

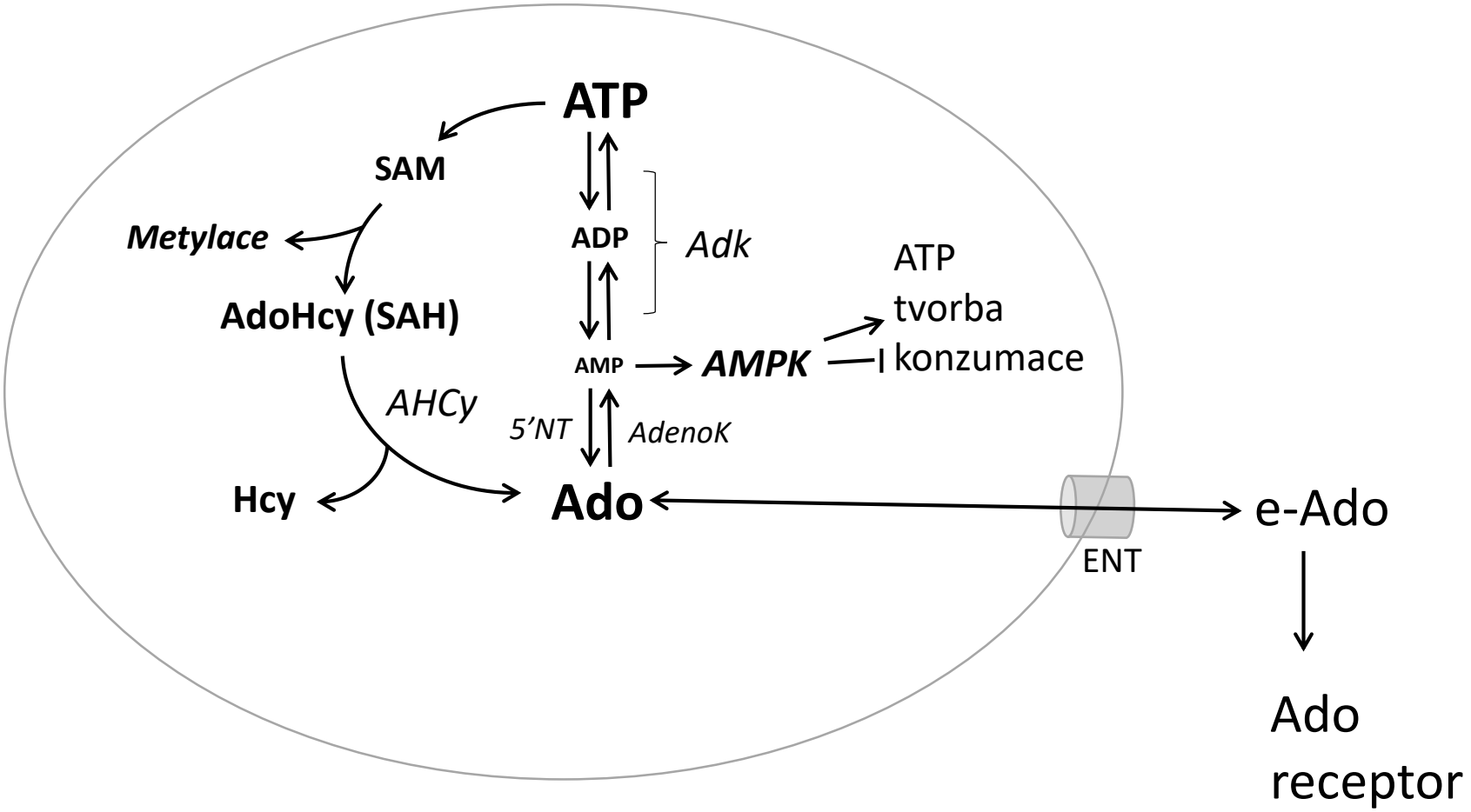
Lactate


Poškození tkáně
únik ATP
buněčný stres
⇩ATP
Hypoxie (anoxie)
svalová aktivita
aktivita mozku
e-Ado
extracelulární adenozin
+ aktivace imunitních buněk?
AdoR
receptor adenozinu
Únava
Spánek
Hibernace
Zpomalení metabolizmu buněk

Proč adenozin?

Měření aktivity buňky?

Měření energetického stavu buňky?



PODĚKOVÁNÍ

Adam Bajgar, **Monika Žuberová, Milena Nováková, Michaela Fencková**

Paul Strasser, Lucie Jonátová, Kateřina Kučerová,, Martina Slapničková, Pavla Šnebergerová

Aleš Tomčala, Ivana Schneedorferová, Jan Okrouhlík

David Schneider and Schneider lab (Stanford University, USA)
Marek Jindra (ENTÚ – BC AVČR, České Budějovice)
Michele Crozatier (Toulouse, Francie)

VDRC, Bloomington Stock Center

GAČR CZECH SCIENCE FOUNDATION **Projekt P305-12-0115**

MARIE CURIE ACTIONS **Marie Curie International Outgoing Fellowship** within the 7th European Community Framework Programme - Project 298186