Typ-2-Diabetes und Adipositas - Forschung für maßgeschneiderte Therapien

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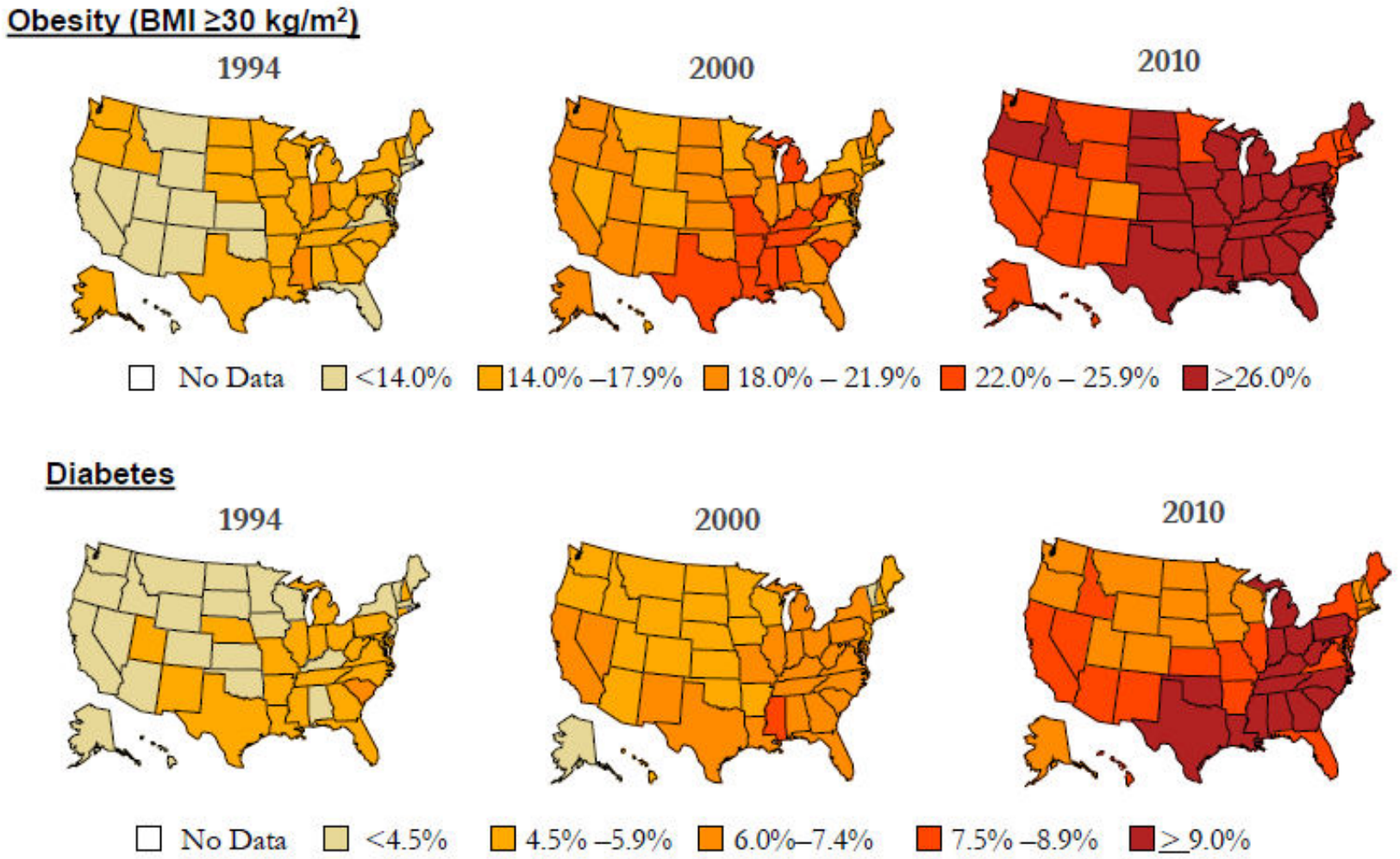
Helmholtz Zentrum München

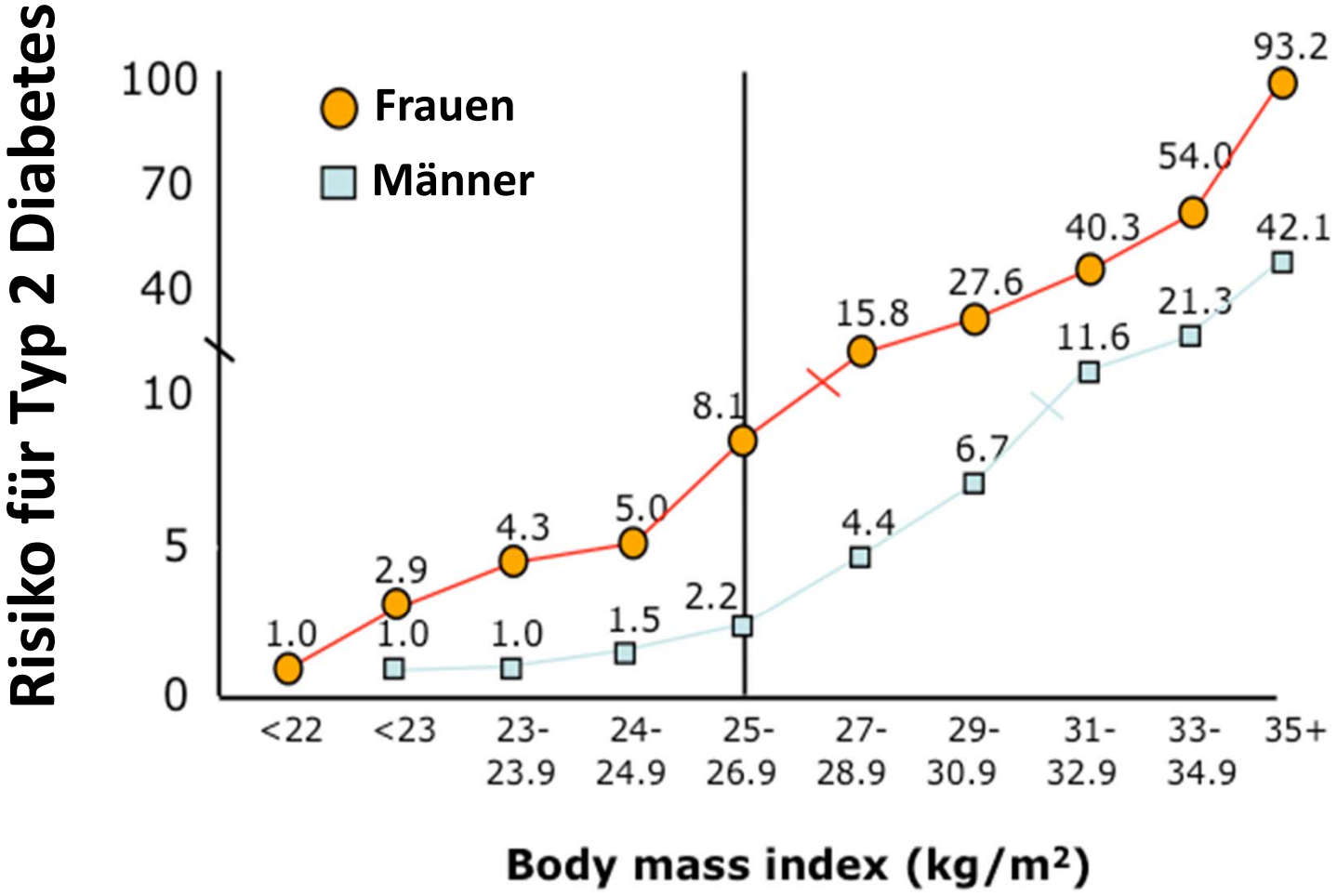
Technical University Munich, Germany

Prävalenz von Adipositas und Diabetes bei U.S. Amerikanern

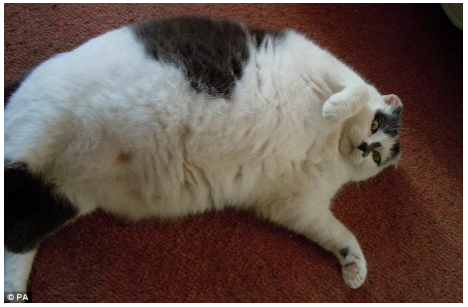


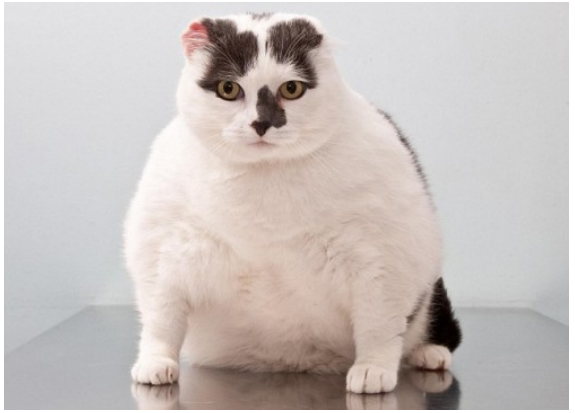
CDC's Division of Diabetes Translation. National Diabetes Surveillance System available at http://www.cdc.gov/diabetes/statistics

Das Diabetesrisiko steigt mit steigendem BMI



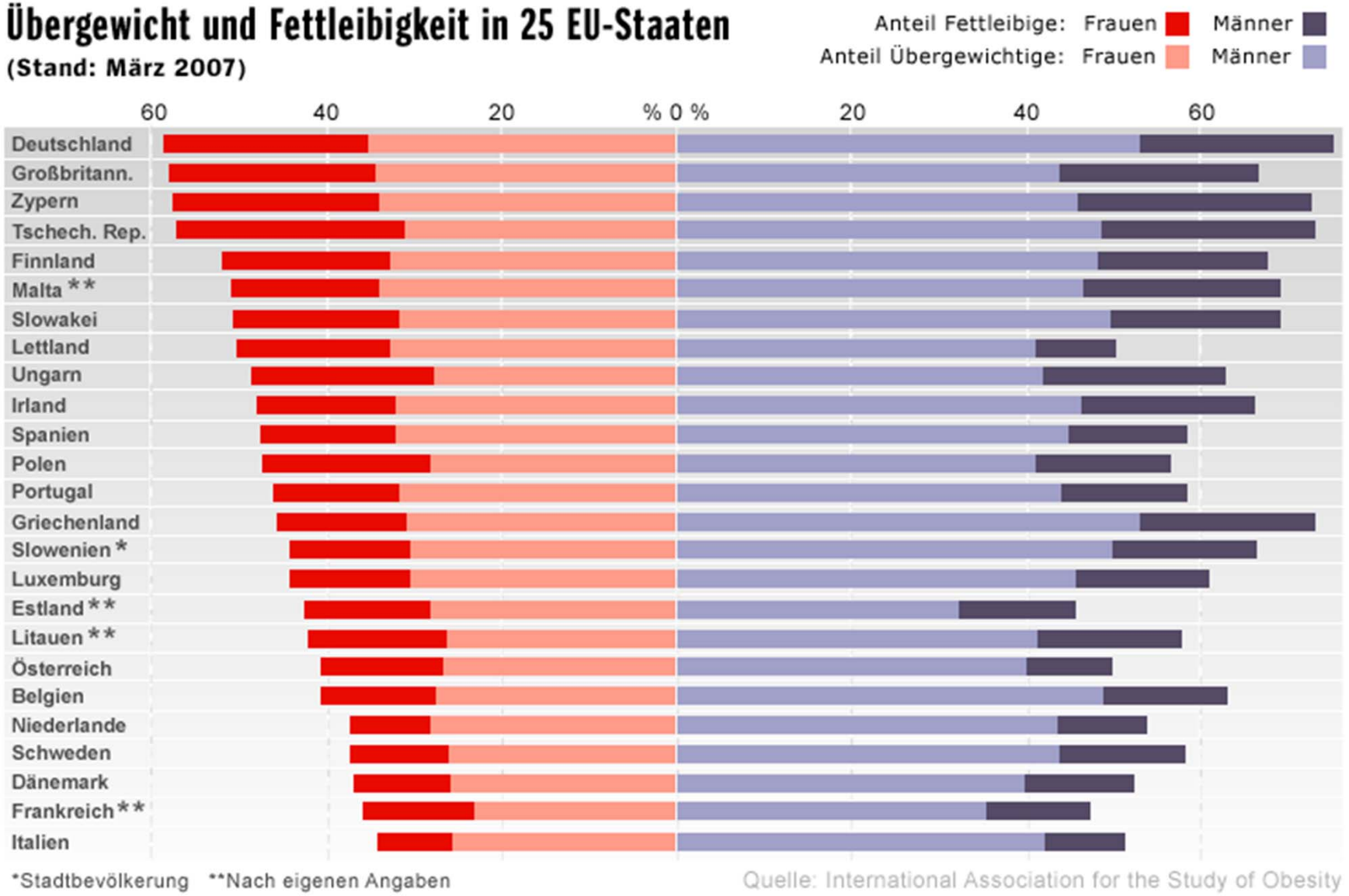
International Diabetes Federation





Übergewicht und Fettleibigkeit in 25 EU-Staaten

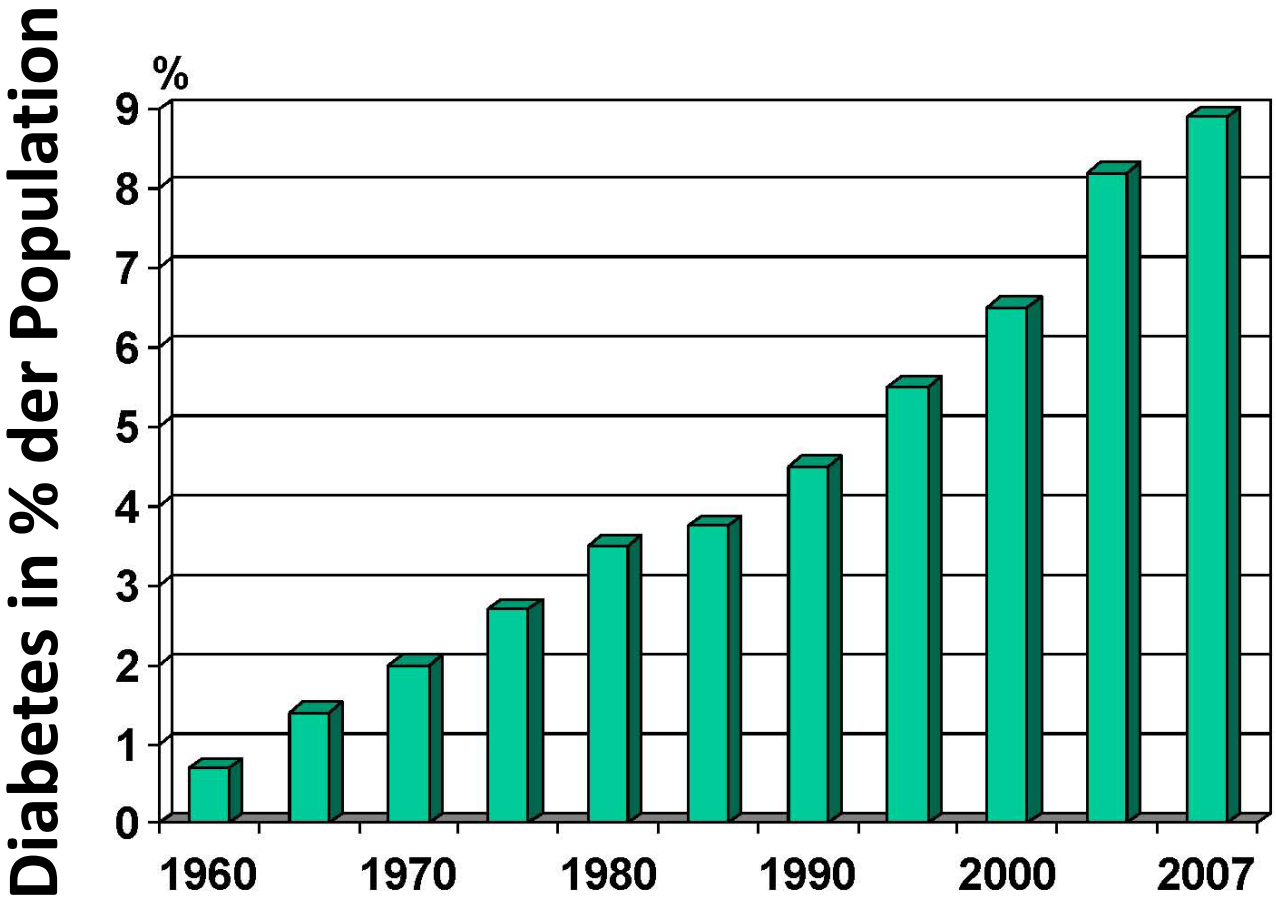
(Stand: März 2007)



*Stadtbevölkerung **Nach eigenen Angaben

Quelle: International Association for the Study of Obesity

Diabetes in Deutschland seit 1960



Michaelis et al., Exp Clin Endocrinol. 1990; Köster et al., PMV 2008

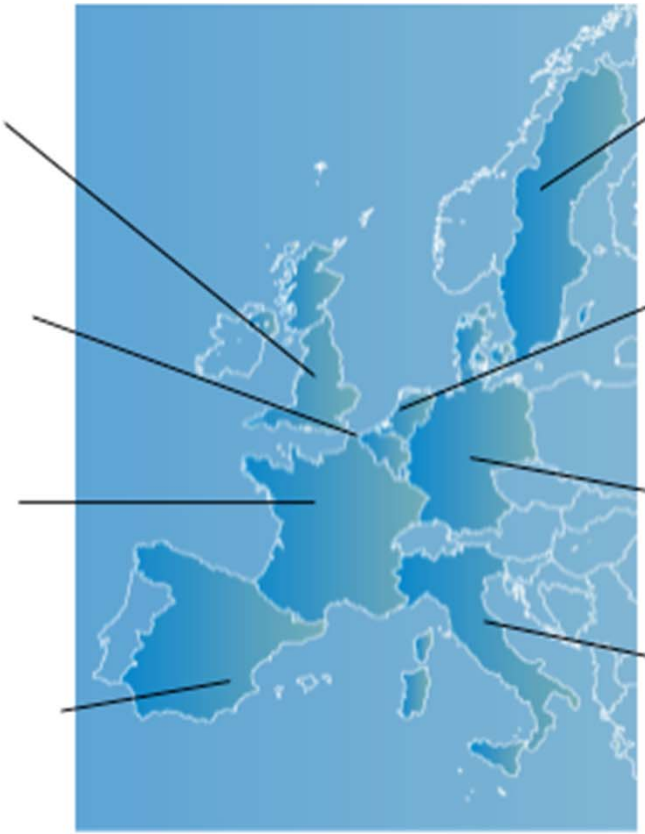
Jährliche direkte Kosten für Typ 2 Diabetes

UK
2,6 Milliarden Euro

Belgien
1,1 Milliarden Euro

Frankreich
4 Milliarden Euro

Spanien
2 Milliarden Euro



Schweden
0,7 Milliarden Euro

Niederlande
0,4 Milliarden Euro

Deutschland
12,4 Milliarden Euro

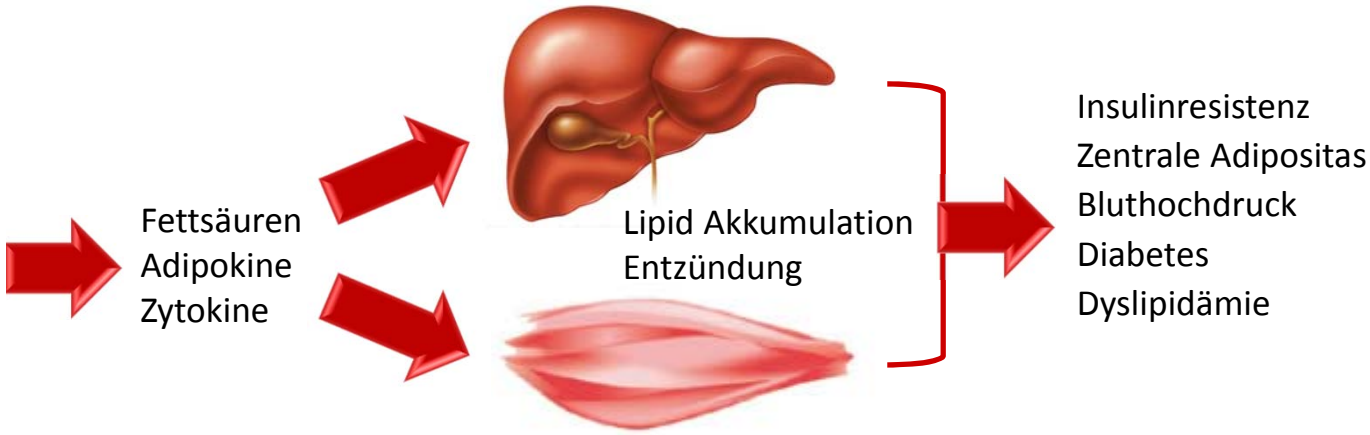
Italien
5,8 Milliarden Euro

Jährliche Gesamtkosten: 29 Milliarden Euro

International Diabetes Federation

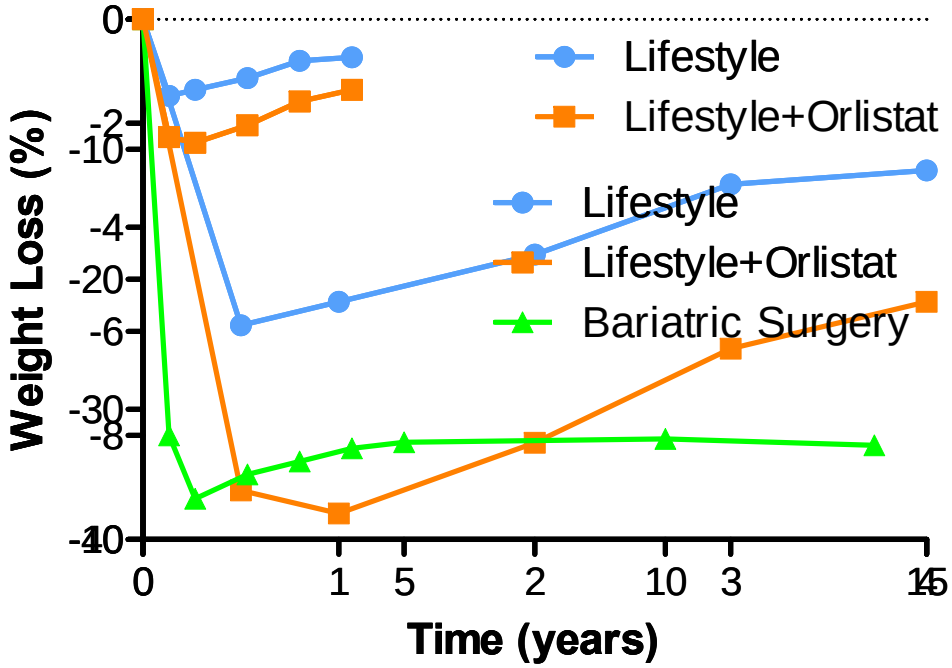
Das Metabolische Syndrom

- **Adipositas**
- **Bluthochdruck**
- **Insulinresistenz**
- **Diabetes**
- **Dyslipidämie**



Verfügbare Adipositas-Therapien

- Diät
- Pharmakologie
- Bariatrische Chirurgie



Adapted from Pories et al., *Ann Surg* 1995
and Torgerson et al., *Diabetes Care* 2004

Pharmafirmen in der Adipositasforschung

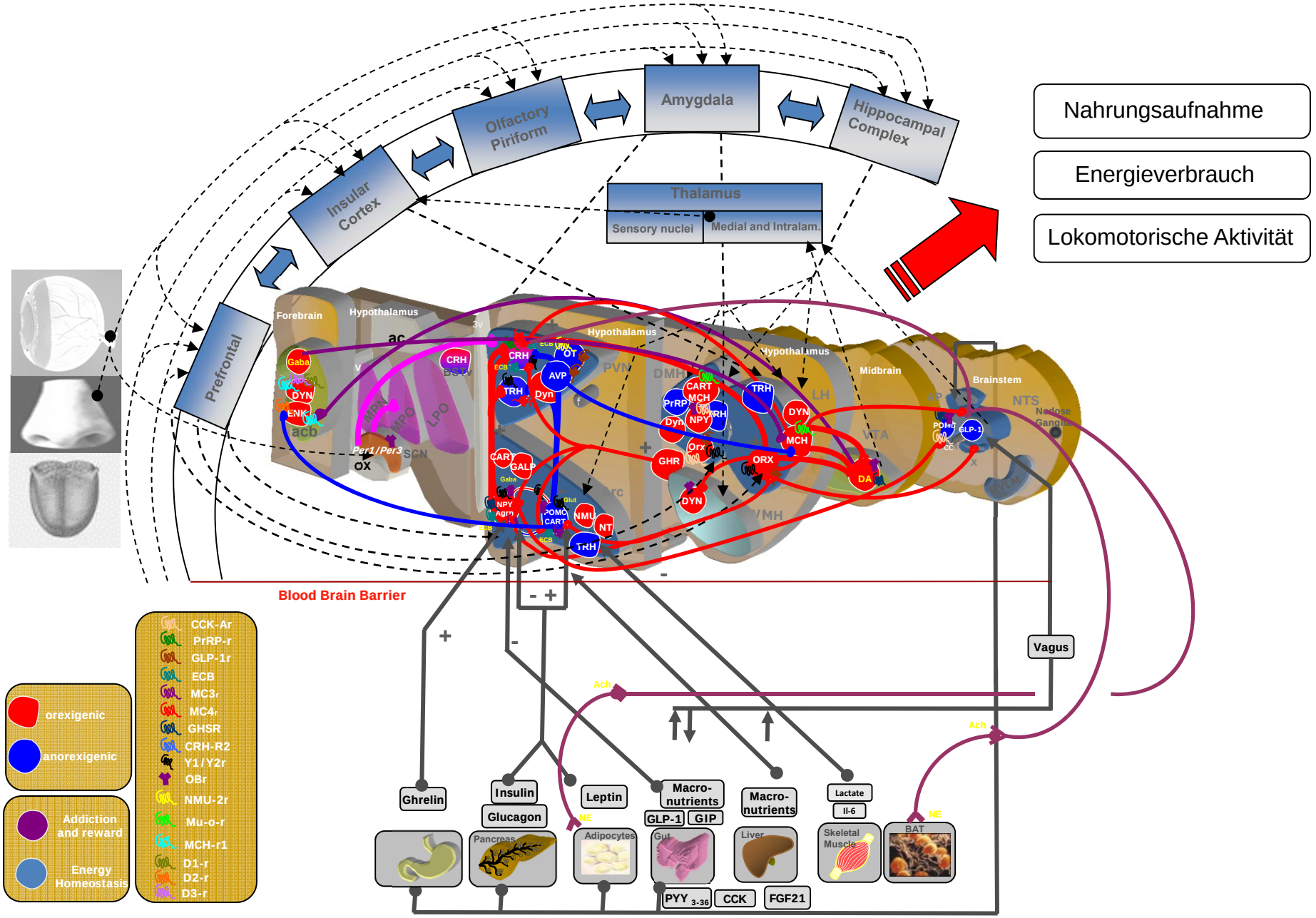
Pharma – circa 1990

- Abbott
- American Cyanamid
- A.H. Robbins
- Astra
- BASF
- Beecham
- Boehringer Ingelheim
- Boots
- Bristol-Myers
- Carter-Wallace
- Ciba-Geigy
- Connaught Labs
- DuPont Pharma
- Fisons Corp.
- Searle
- Glaxo
- Hoechst
- Roche
- ICI
- J & J
- Knoll
- Eli Lilly
- Marion Labs
- Merck
- Merrell Dow
- Novo Nordisk
- Pfizer
- Pharmacia
- Procter & Gamble
- Rhone Poulenc
- Rorer
- Scherer
- Roussel
- Sandoz
- Schering-Plough
- SmithKline
- Squibb
- Sterling
- Upjohn
- Warner-Lambert
- Wellcome
- Zeneca

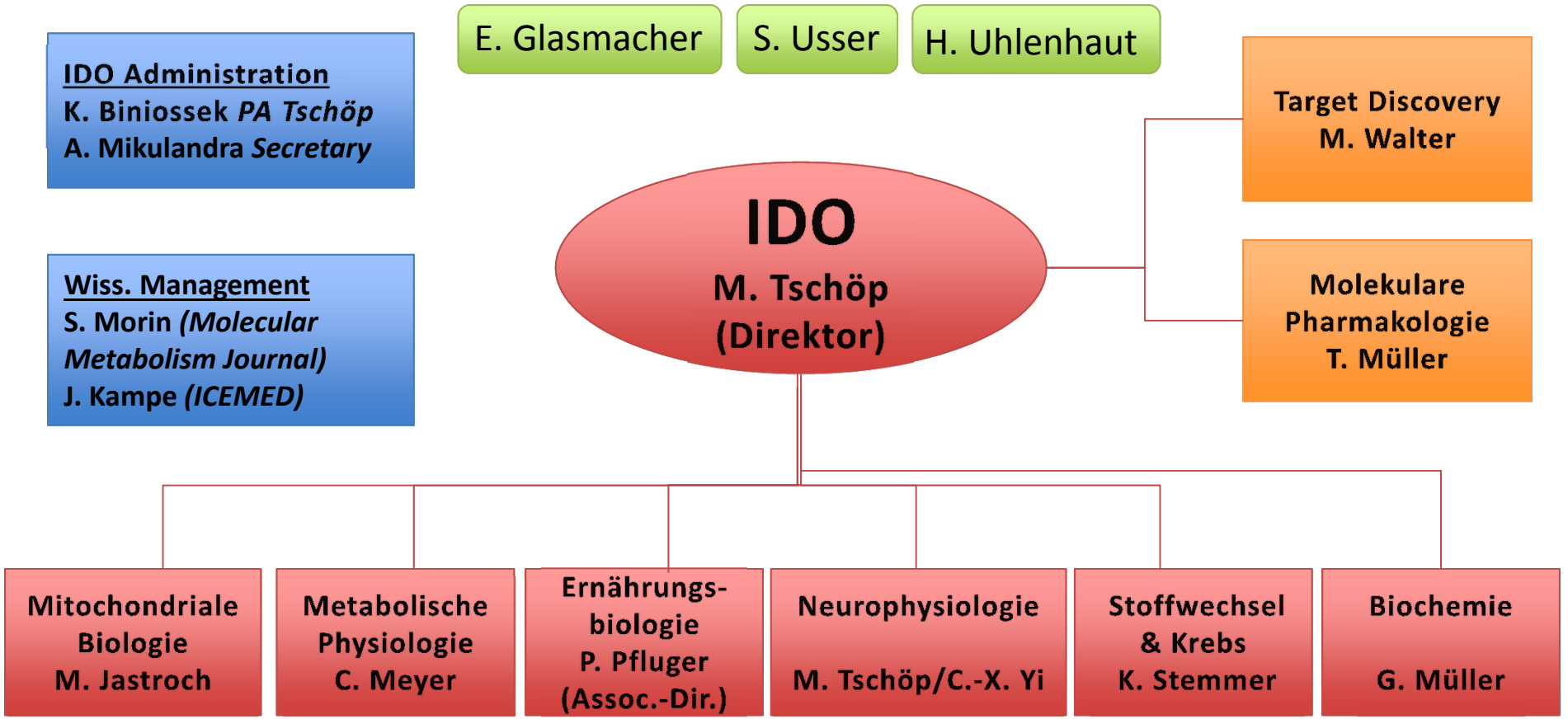
Pharmafirmen in der Adipositasforschung

Pharma – Heute

- Abbott
- AstraZeneca
- BASF
- B. Ingelheim
- Bristol-Myers
- Glaxo
- Roche
- J & J
- Eli Lilly
- Merck
- Novartis
- Novo Nordisk
- Pfizer
- Sanofi


Nahrungsaufnahme
Energieverbrauch
Lokomotorische Aktivität
Amygdala
Olfactory Piriform
Hippocampal Complex
Insular Cortex
Prefrontal
Thalamus
Sensory nuclei
Medial and Intralam.
Forebrain
Hypothalamus
Midbrain
Brainstem
Blood Brain Barrier
Vagus
Ach
NE
Ghrelin
Insulin
Glucagon
Leptin
Macro-nutrients
GLP-1
GIP
Macro-nutrients
Lactate
Il-6
PYY 3-36
CCK
FGF21
Pancreas
Adipocytes
Gut
Liver
Skeletal Muscle
BAT
orexigenic
anorexigenic
Addiction and reward
Energy Homeostasis
CCK-Ar
PrRP-r
GLP-1r
ECB
MC3r
MC4r
GHSR
CRH-R2
Y1/Y2r
OBr
NMU-2r
Mu-o-r
MCH-r1
D1-r
D2-r
D3-r

Das Institut für Diabetes and Adipositas (IDO)

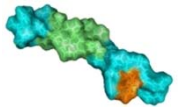


Ziel: Entwicklung neuer Therapien zur effektiven und sicheren Behandlung von Adipositas und Diabetes

Kombination endogener Hormone

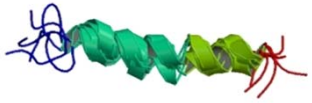
Hormon 1:

inhibiert
Nahrungsaufnahme &
verbessert Insulinsekretion



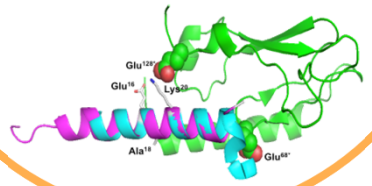
Hormon 2:

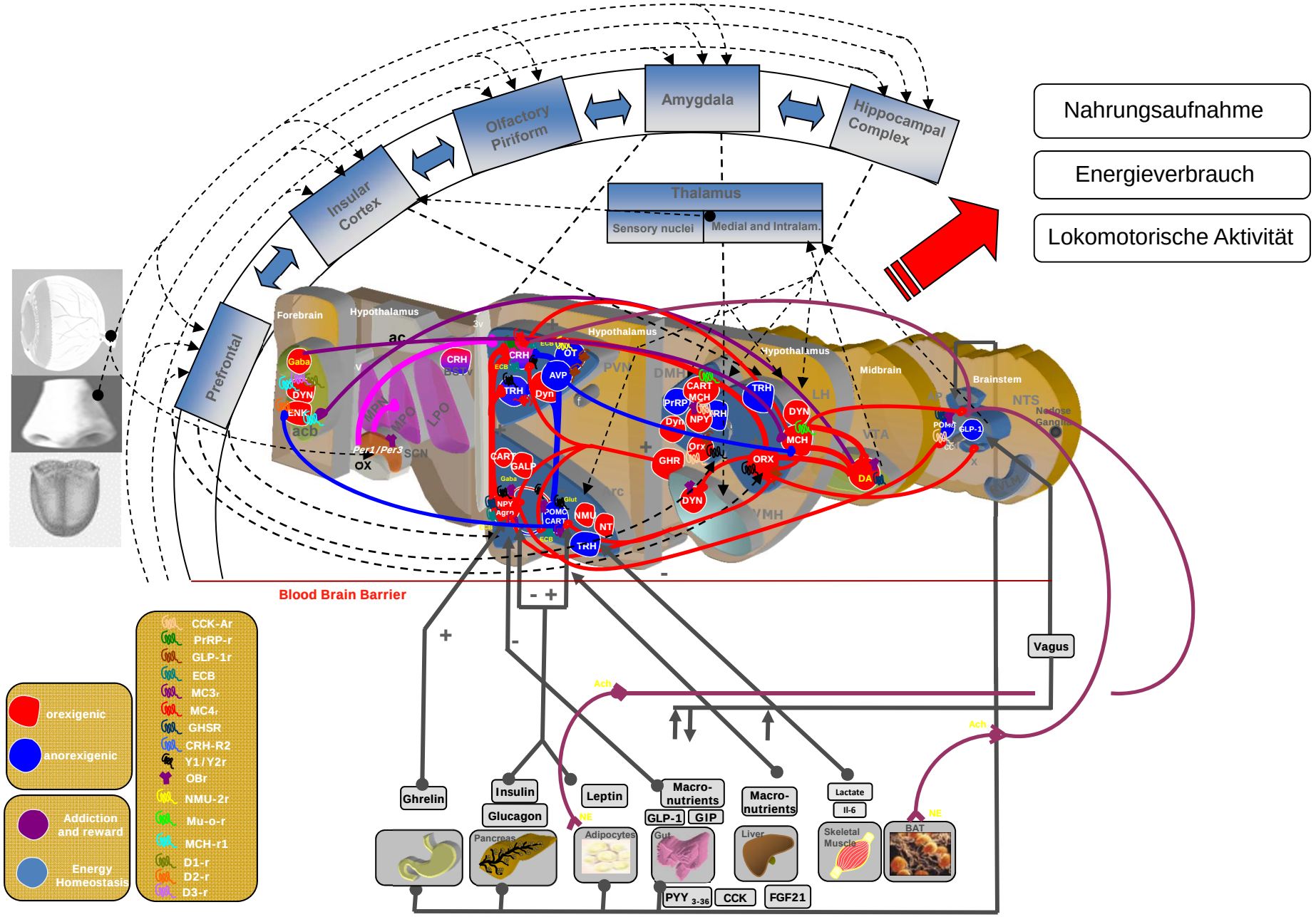
Erhöht Energieverbrauch



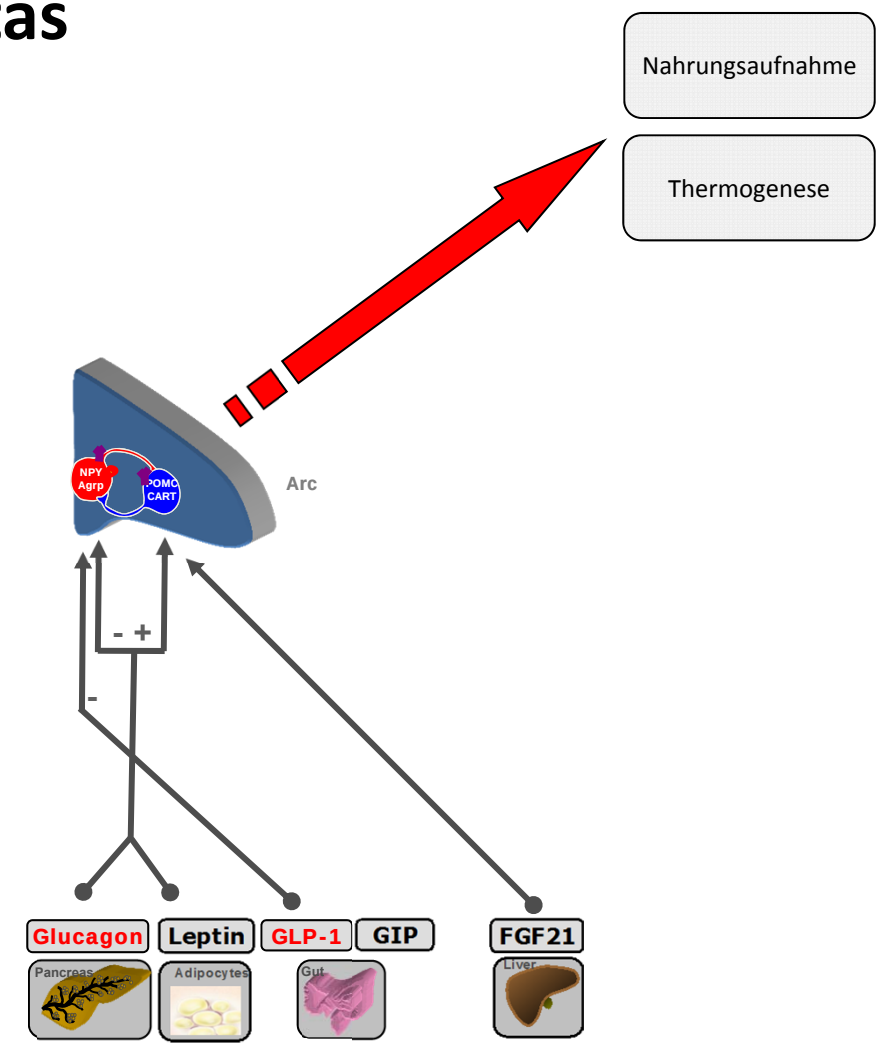
Einzel-Molekül

Co-Agonist

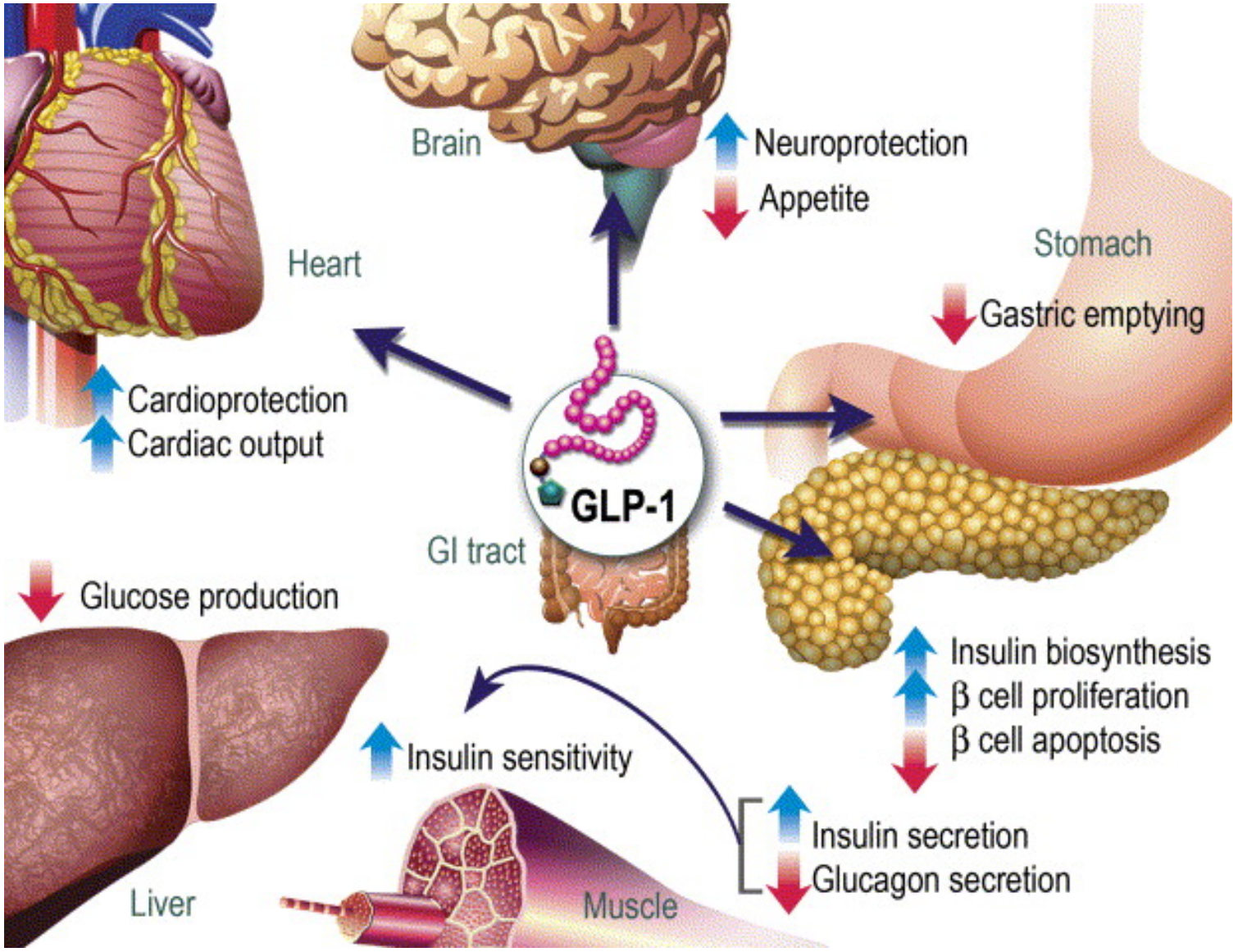



Nahrungsaufnahme
Energieverbrauch
Lokomotorische Aktivität
Amygdala
Olfactory Piriform
Hippocampal Complex
Insular Cortex
Prefrontal
Thalamus
Sensory nuclei
Medial and Intralam.
Forebrain
Hypothalamus
Midbrain
Brainstem
Blood Brain Barrier
Vagus
Ach
NE
Ghrelin
Insulin
Glucagon
Leptin
Macro-nutrients
GLP-1
GIP
Macro-nutrients
Lactate
Il-6
PYY 3-36
CCK
FGF21
Pancreas
Adipocytes
Gut
Liver
Skeletal Muscle
BAT
orexigenic
anorexigenic
Addiction and reward
Energy Homeostasis
CCK-Ar
PrRP-r
GLP-1r
ECB
MC3r
MC4r
GHSR
CRH-R2
Y1/Y2r
OBr
NMU-2r
Mu-o-r
MCH-r1
D1-r
D2-r
D3-r

Co-Agonisten als neue Strategie für Adipositas und Diabetes



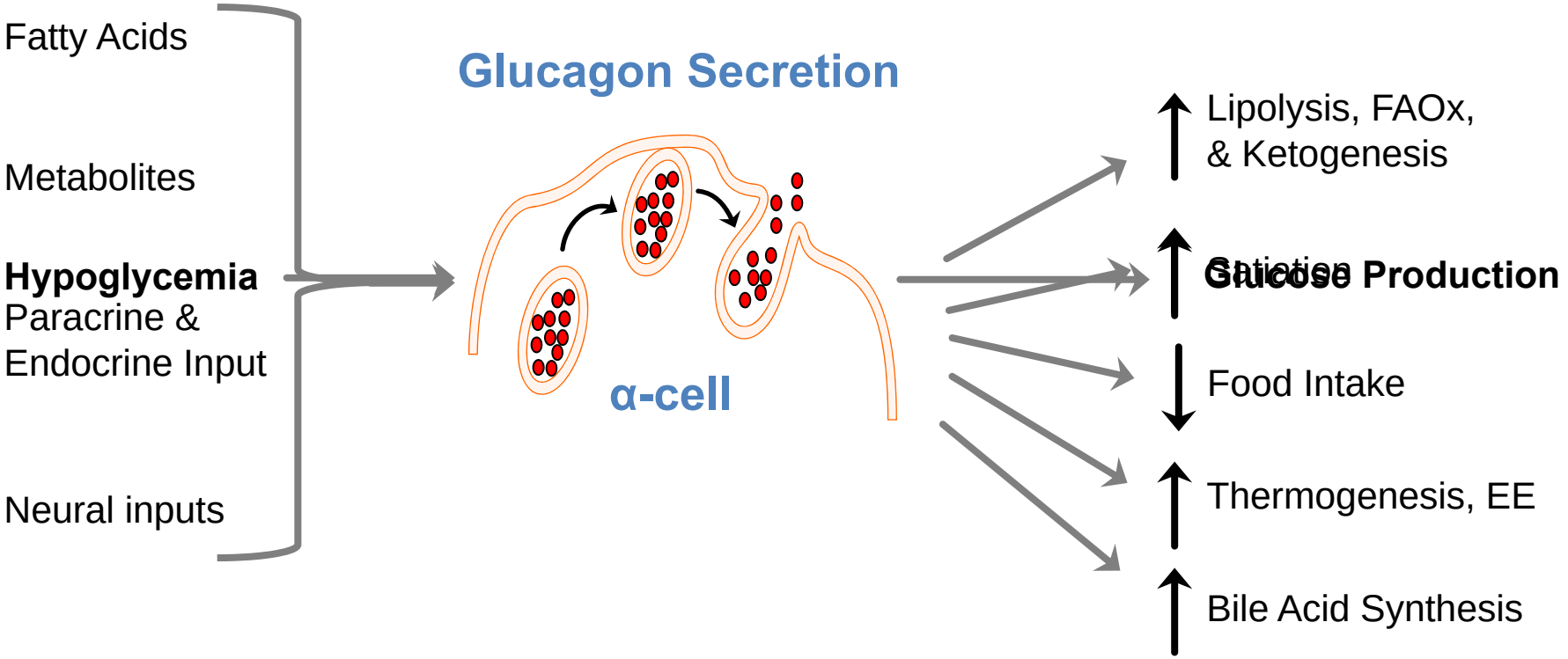
Hormon 1: GLP-1



Drucker, D. Cell Metabolism. 2006; 3:153-165

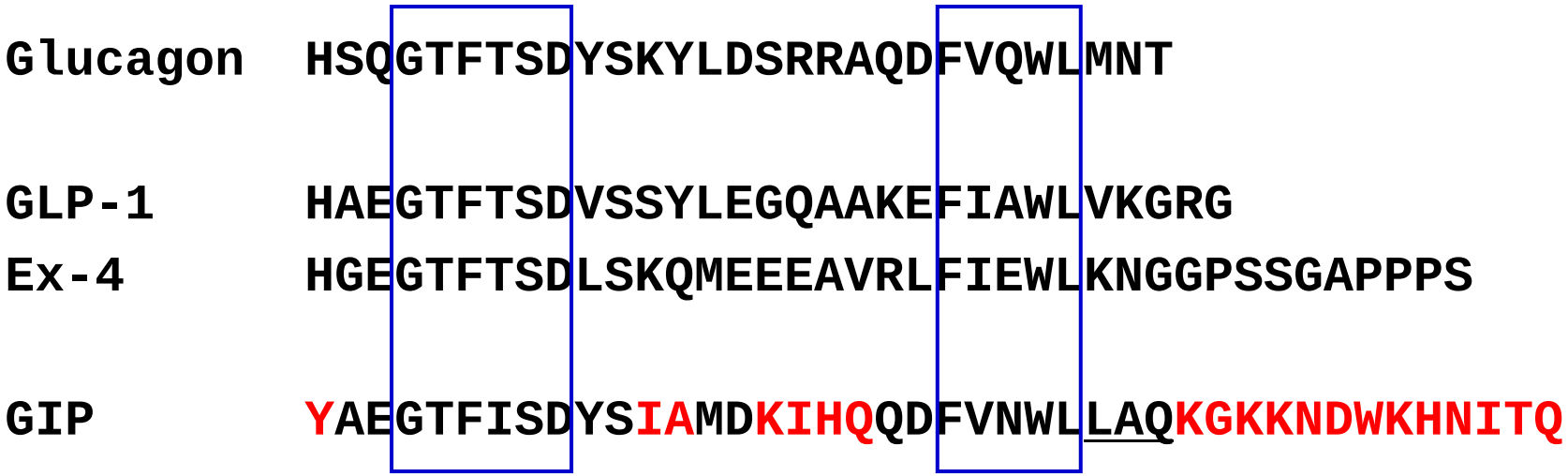
Hormon 2: Glucagon

Glucagon

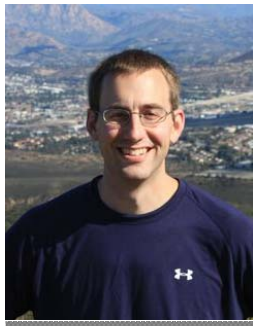


Habegger et al., *Nature Reviews Endocrinology,* 2010

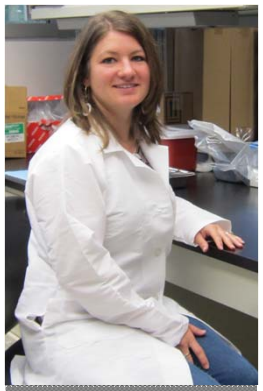
Die Glukagon Familie: Glukagon, GLP-1 and GIP



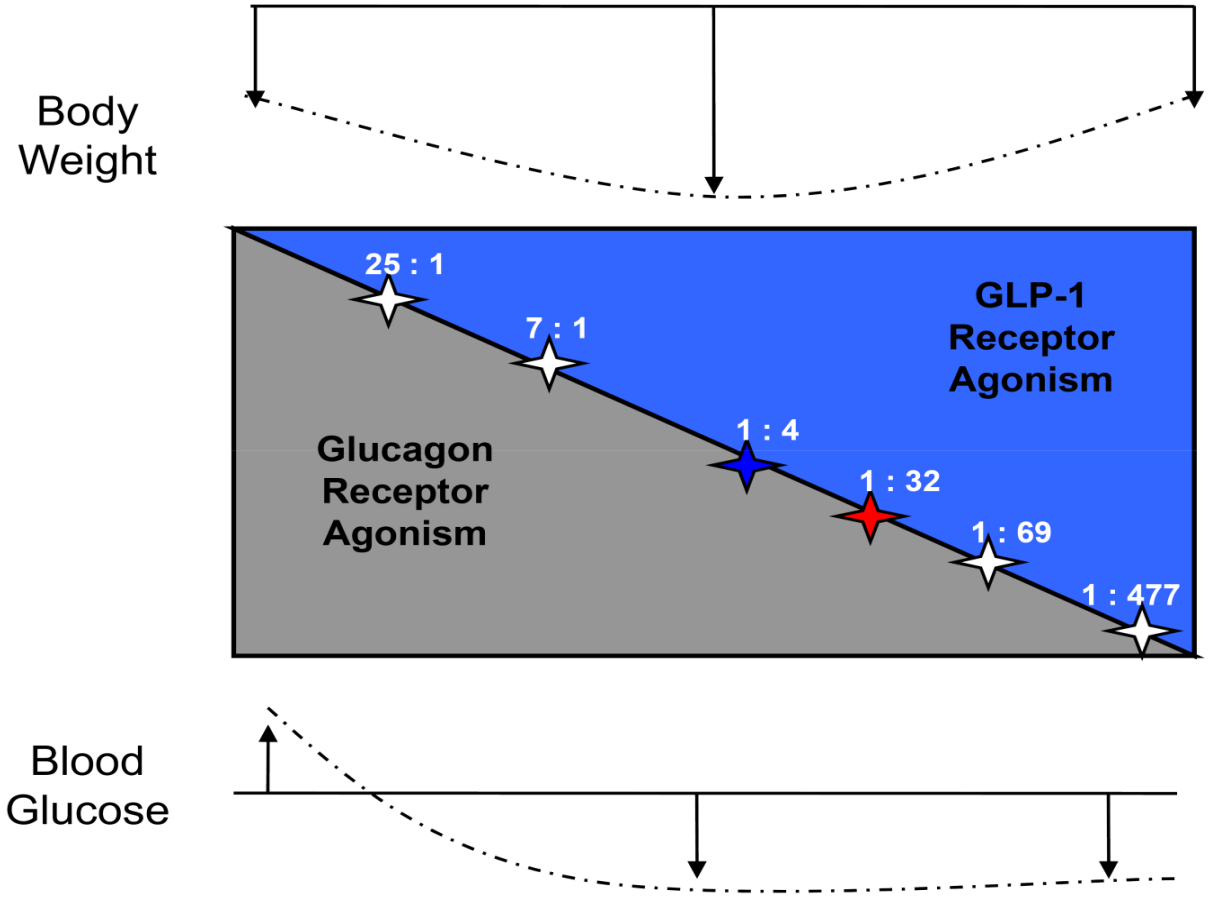
Selektion balancierter GLP1/Glukagon Co-Agonisten für die Behandlung von Adipositas und Diabetes



Jonathan



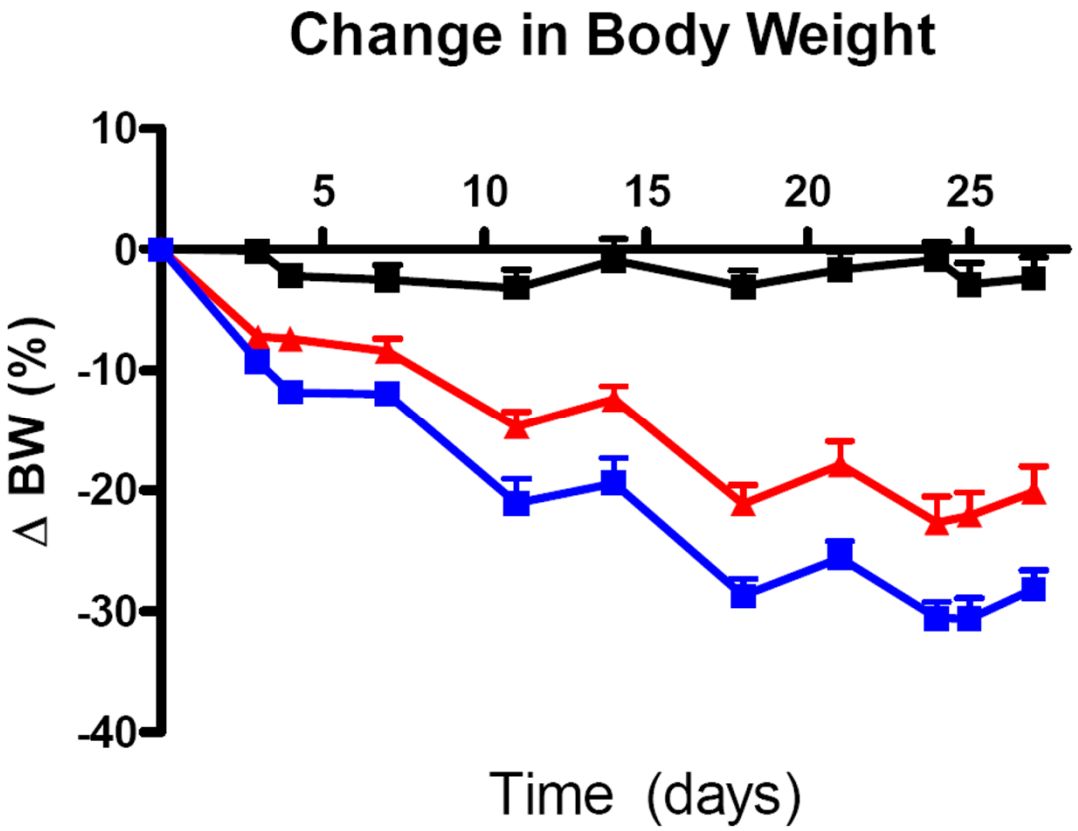
Nickki Ottaway



Day, et al. Nature Chem Biol 2009

Langzeitbehandlung mit GLP-1/glukagon Co-Agonist korrigiert Adipositas

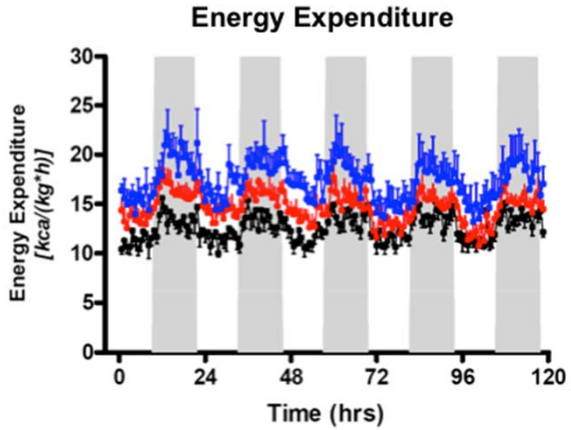
(weekly injection, **one month**, 70 nmol/kg/wk)



Vehicle

Co-agonist 1

Co-agonist 2



Day, et al. *Nature Chem Biol,* 2009

Langzeitbehandlung mit GLP-1/glukagon Co-Agonist korrigiert Adipositas

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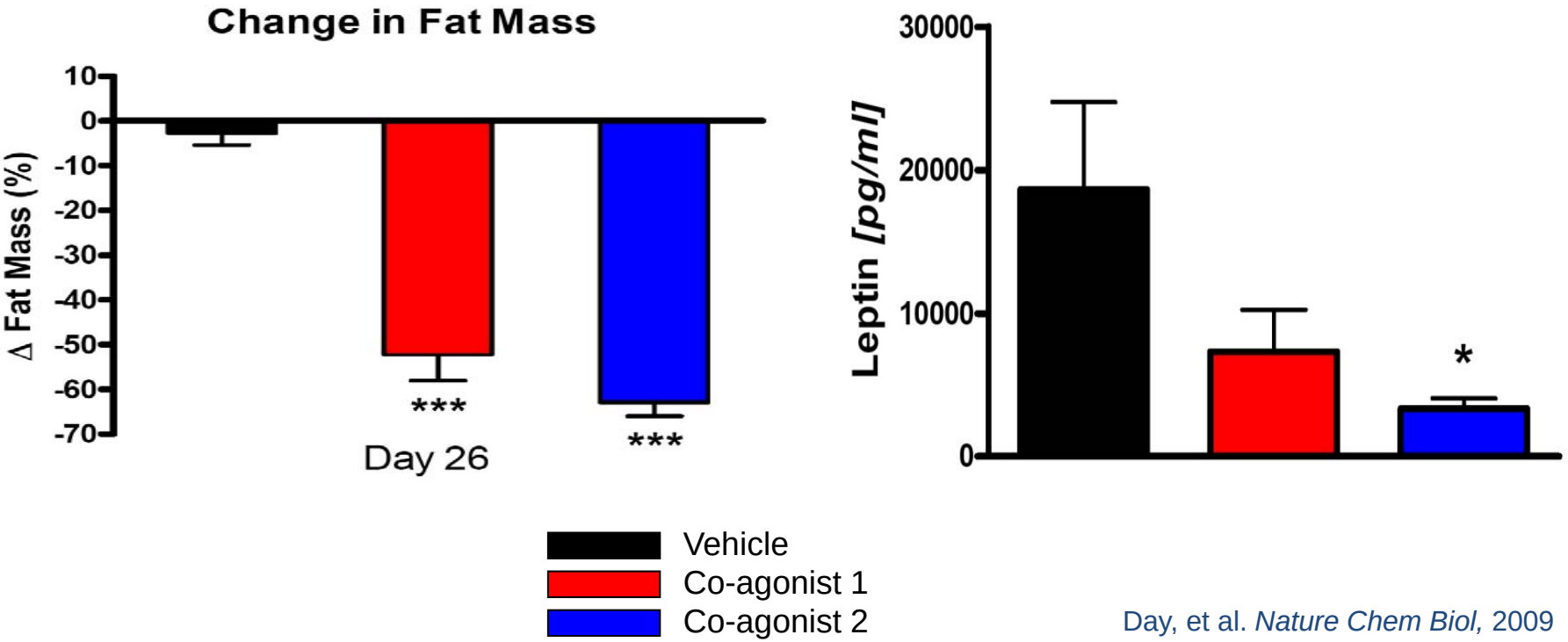
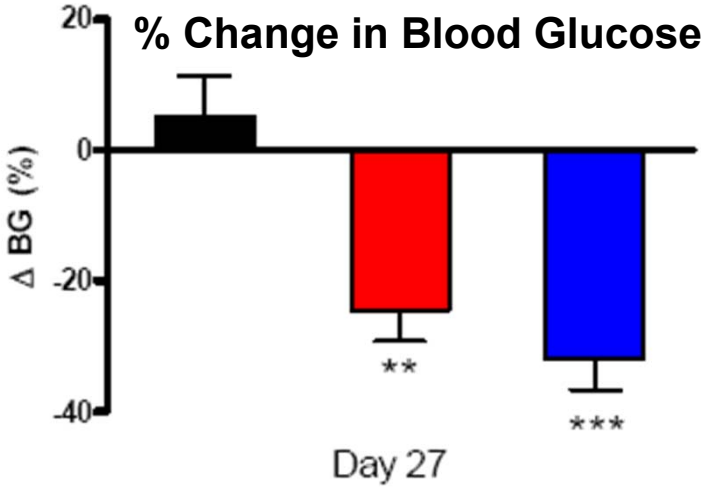
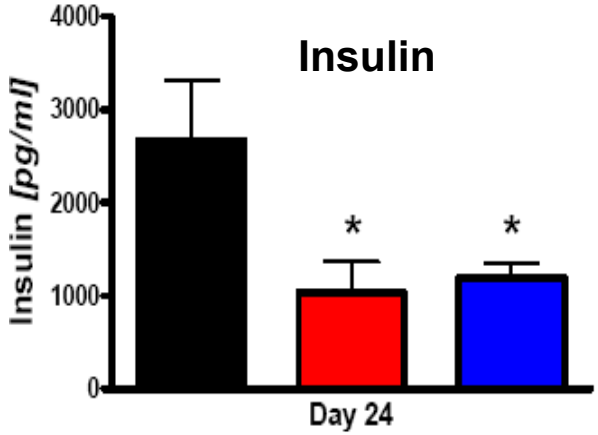


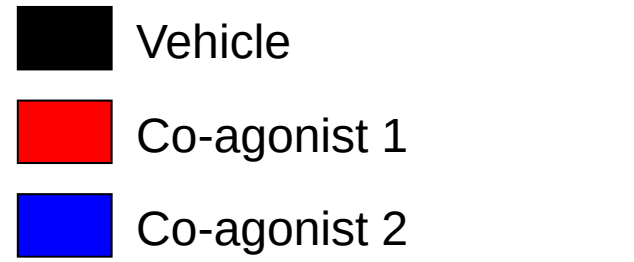
Day, et al. *Nature Chem Biol,* 2009

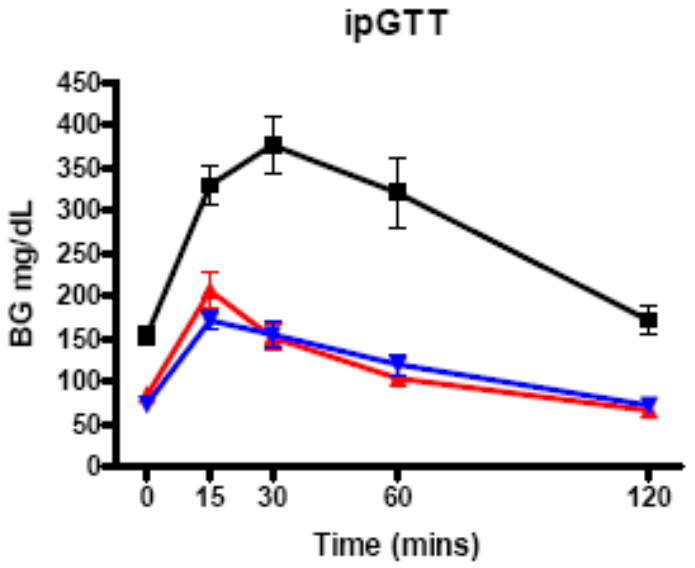
Langzeitbehandlung mit GLP-1/glukagon Co-Agonist verbessert Glukosetoleranz

(weekly injection, **one month**, 70 nmol/kg/wk)



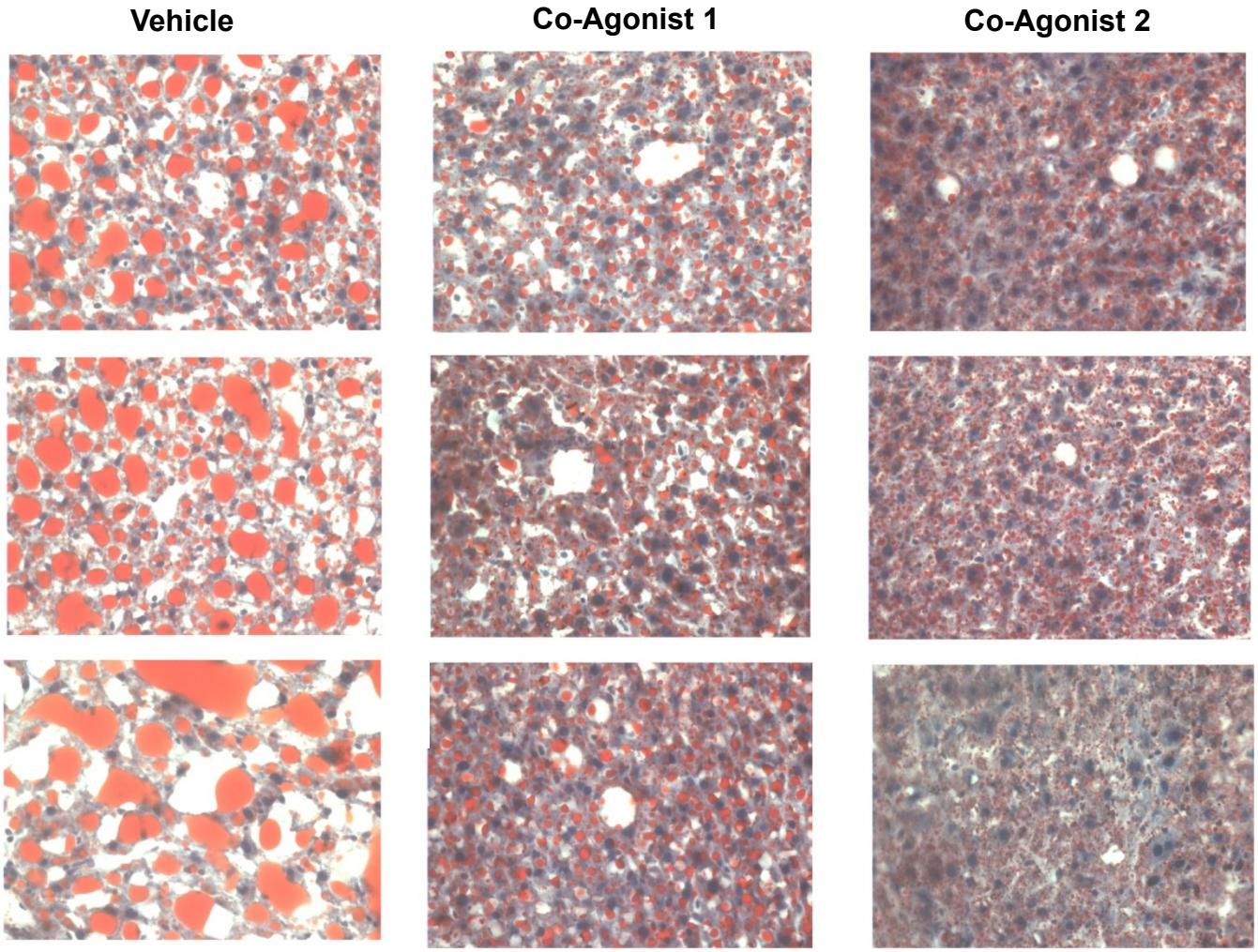






Day, et al. *Nature Chem Biol* 2009

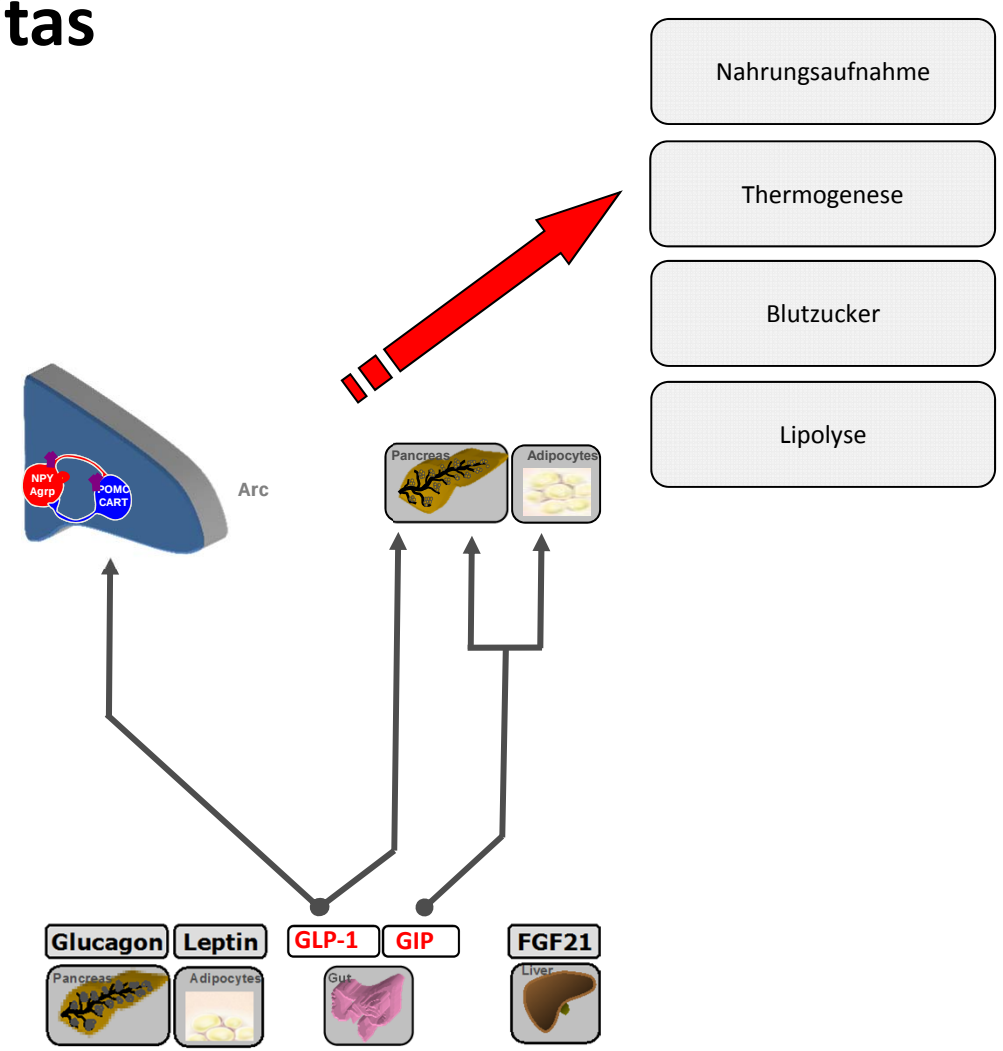
Langzeitbehandlung mit GLP-1/glukagon Co-Agonist verringert Leberverfettung



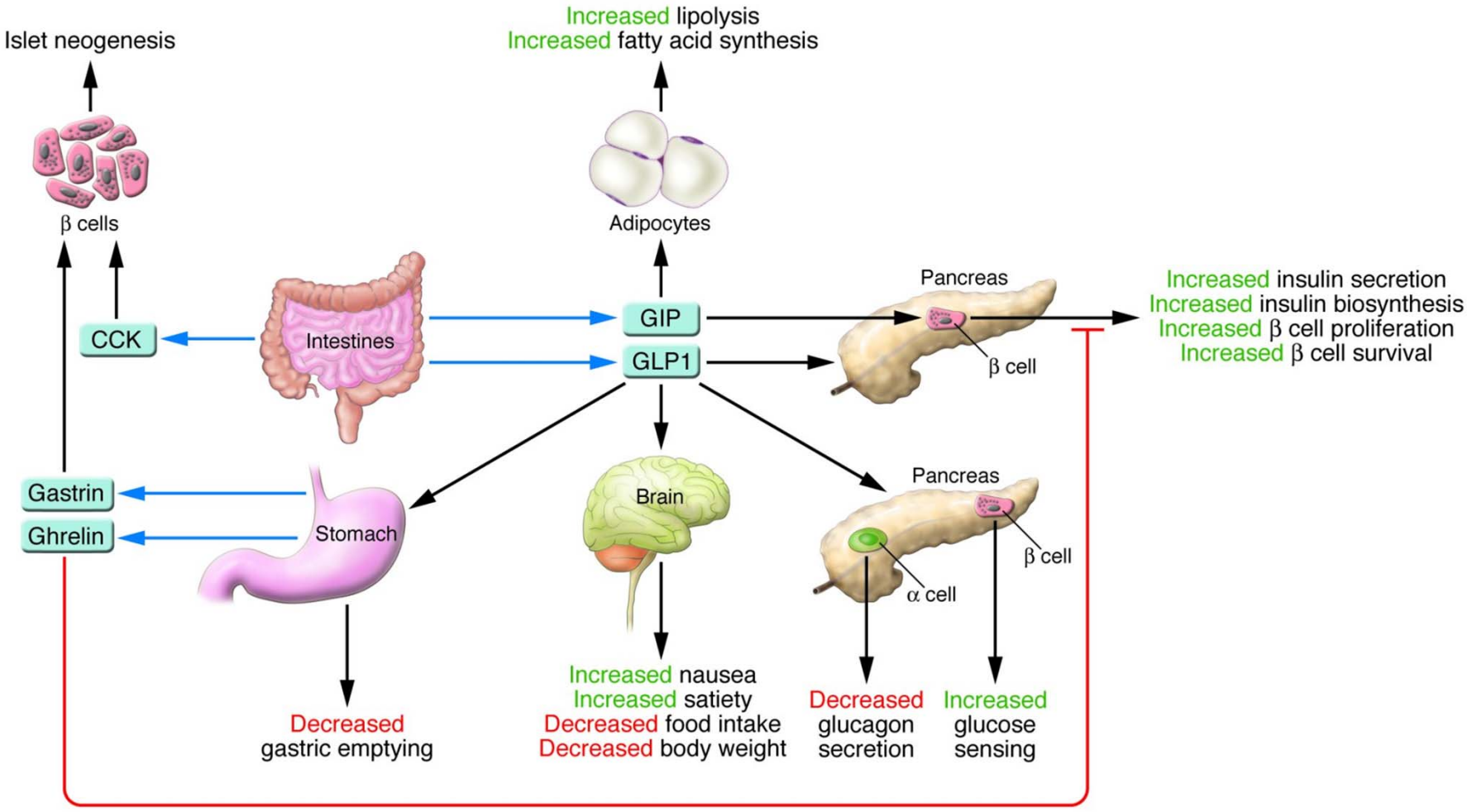
(weekly injection, one month, 70 nmol/kg/wk)

Day, et al. *Nature Chem Biol,* 2009

Co-Agonisten als neue Strategie für Adipositas und Diabetes



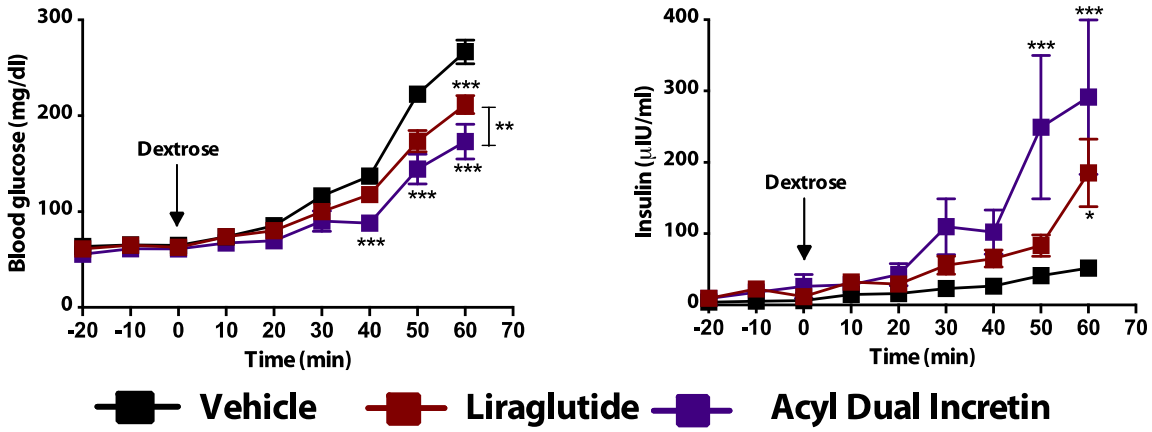
Glp-1/GIP Co-Agonist



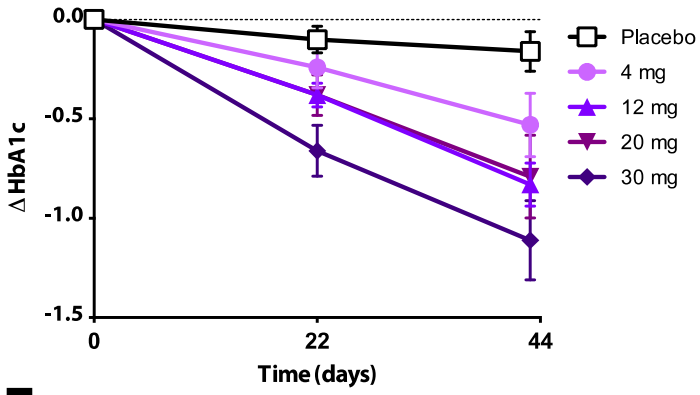
Drucker D, *JCI,* 2007

Dual-Inkretin (GLP-1/GIP) Co-Agonist

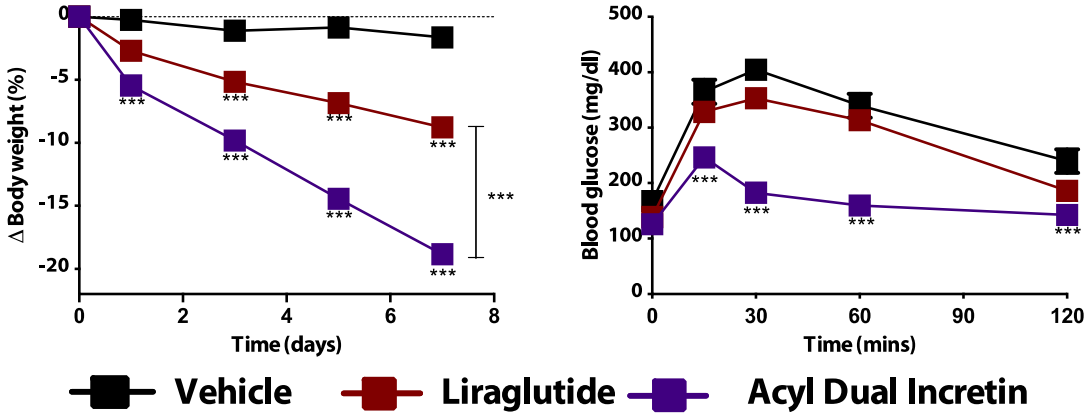
Rhesusaffe

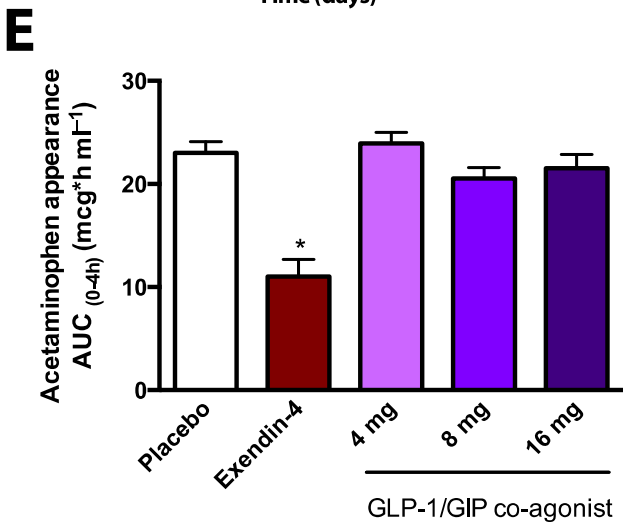


Mensch

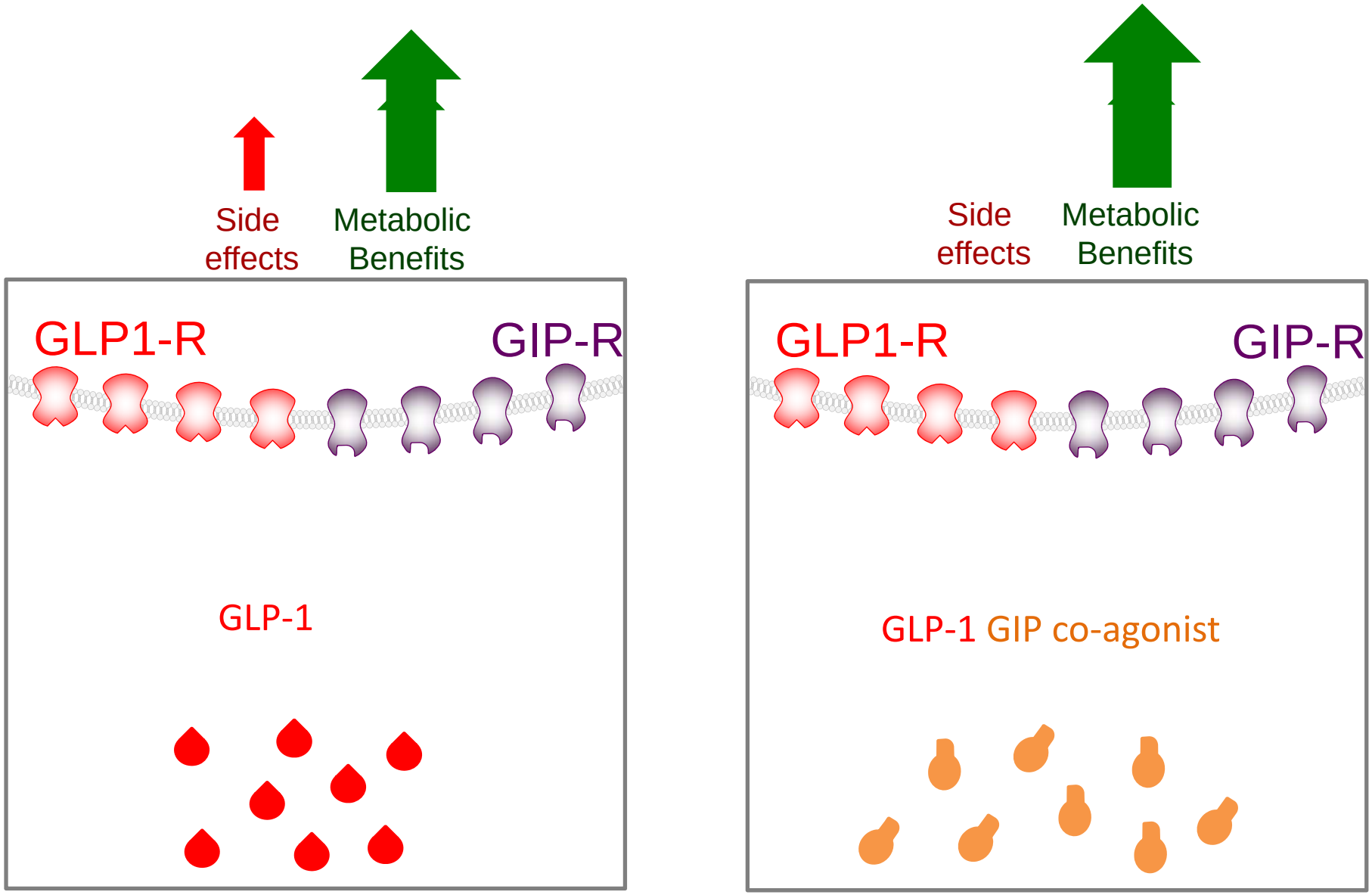


Maus





Finan et al., Sci Transl Med. 2013


Side effects
Metabolic Benefits
GLP1-R
GIP-R
GLP-1
Side effects
Metabolic Benefits
GLP1-R
GIP-R
GLP-1 GIP co-agonist

Acknowledgements

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Hans-Georg Joost
Robert Schwenk
Christian Baumeier
Oliver Kluth
Reinhart Kluge

Pre-Clinical Contractors

SEVENTHWAVE
MEDPACE