Rund 1000

→ Mitarbeitende stehen täglich bei uns im Einsatz.

Stellenwert des Fastens und der ketogenen Diät in der Onkologie

Dr.med. Donat Dürr, Leiter Onkologie ZGKS

ZUGER Kantonsspital

E-Mail von Maja Dorfschmid

E-Mail von Maja Dorfschmid

Pluspunkte:

- Für Patientinnen relevantes Thema
- Für mich günstige Gelegenheit, mich weiterzubilden

Negativpunkte:

- Mir wenig geläufiges, breites Thema; grosser Aufwand
- Vorurteil: Wissenschaftlich schlecht untersucht

Uebersicht

- Theoretische Grundlagen des Fastens
- Unterschied gesunde Zelle versus Krebszelle
- Tierversuche
- Humanversuche
- Ketogene Diät

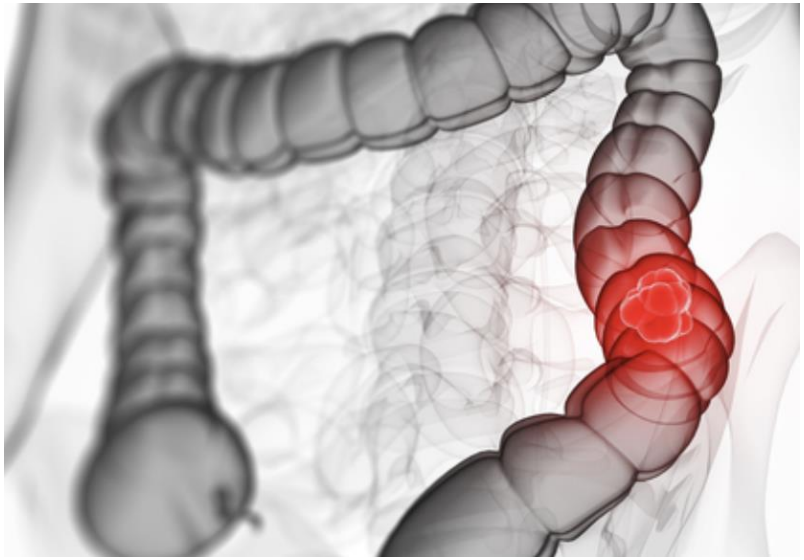
Assoziation: Fasten = Gesund !?

© Can Stock Photo

Dieser Gedanke ist tief im Menschen verankert

Assoziation: Fasten = Gesund !?

Ernährung hat einen Einfluss auf die Gesundheit !

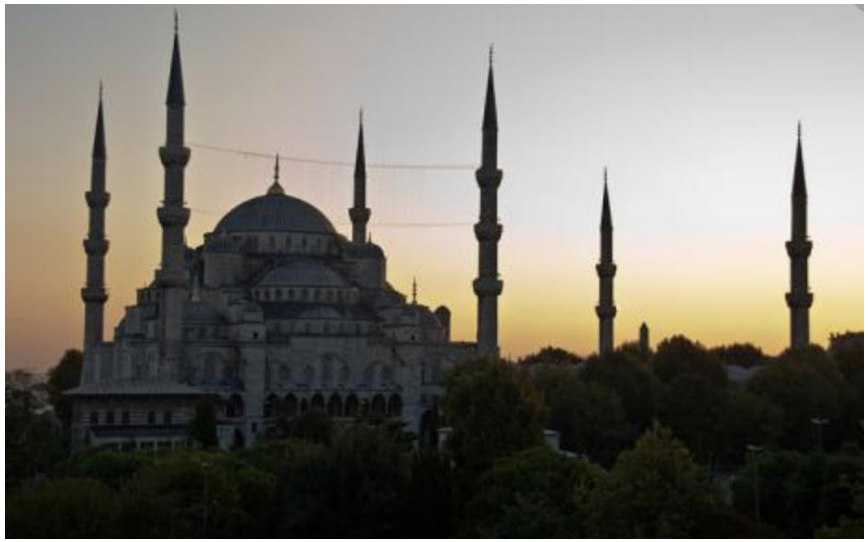


Assoziation: Fasten = Gesund !?

Übermässige Kalorienzufuhr / Adipositas / fehlende Bewegung haben ebenfalls einen Einfluss auf die Gesundheit !

Assoziation: Fasten = Gesund !?

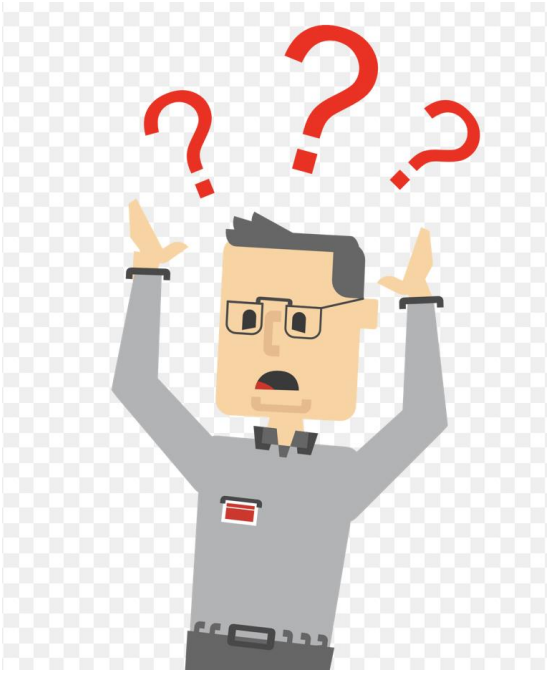
Fasten = Zustand, der tief im Menschen verankert ist



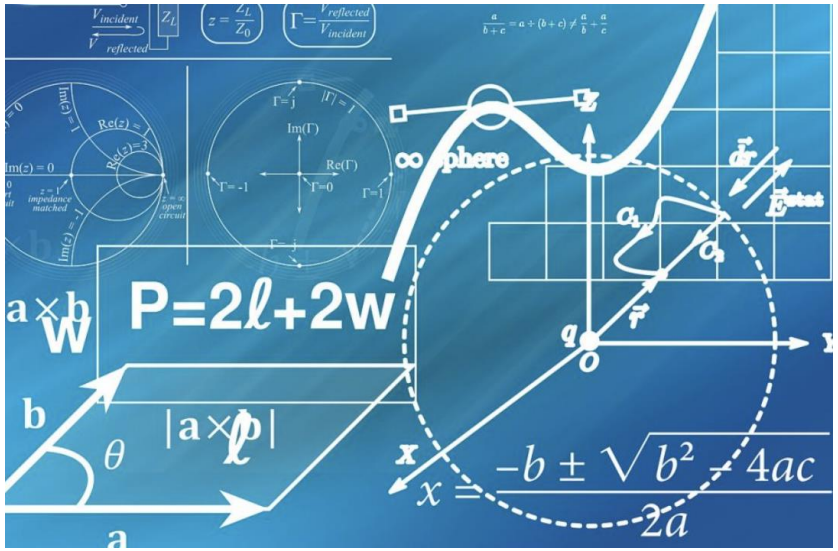
Einführende Gedanken

Fasten / Diäten ⟶ gesundheitlicher Nutzen ?

© Can Stock Photo

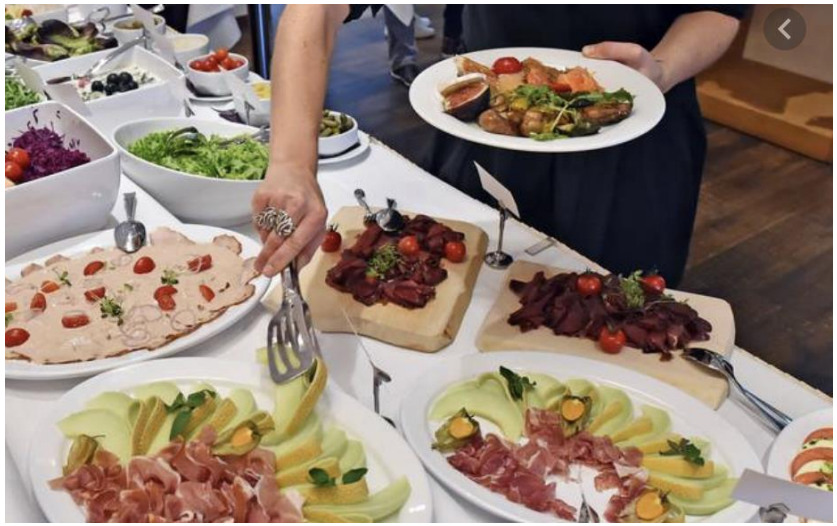


Energieversorgung einer Zelle

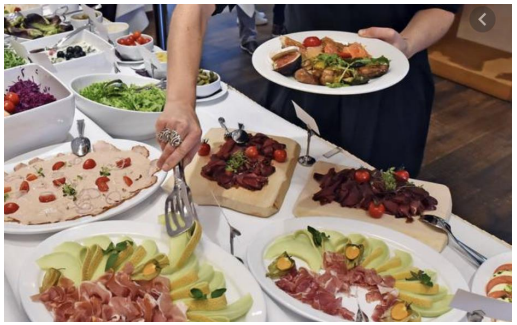


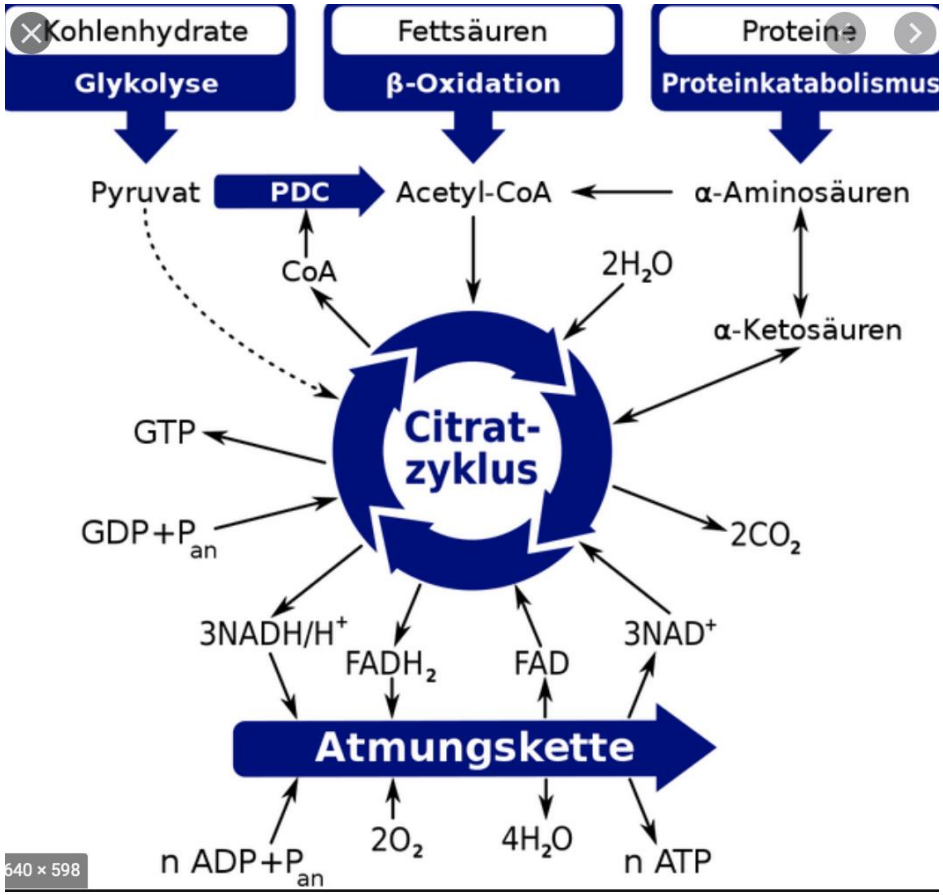
Energieversorgung einer Zelle

2 Zustände



Energieversorgung einer Zelle

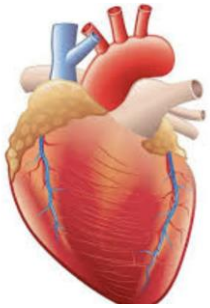


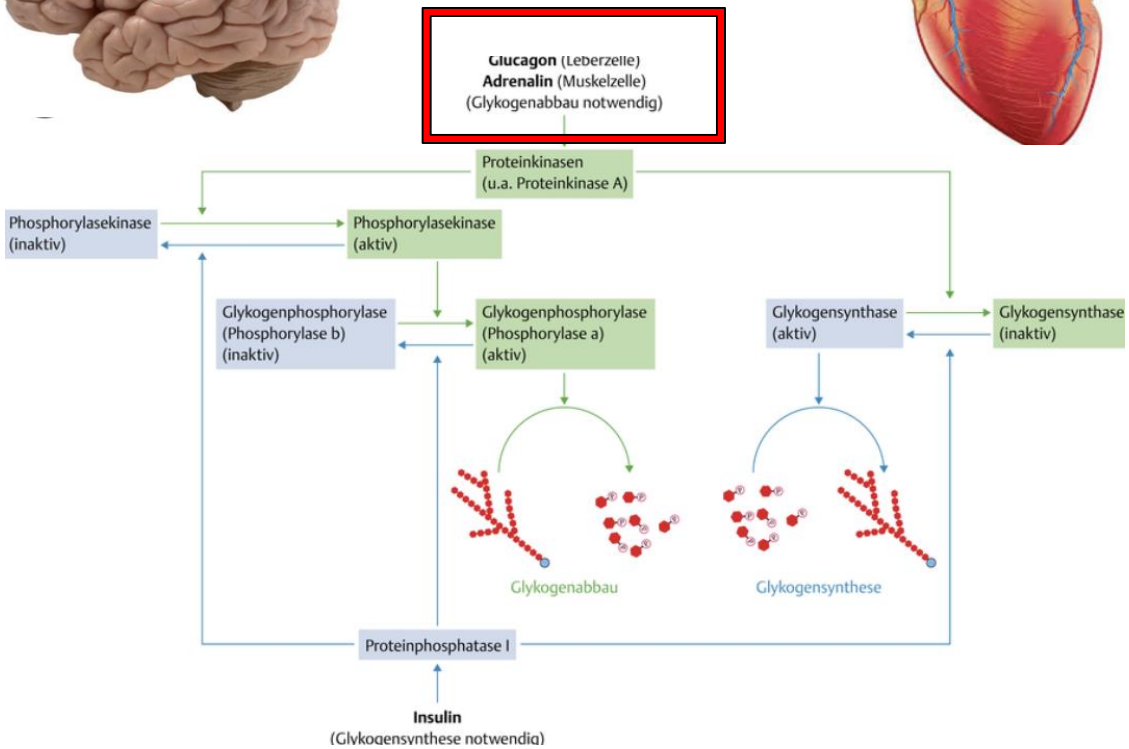


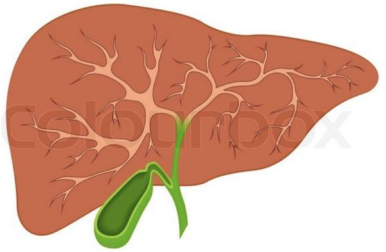
In den Mitochondrien: ATP-Produktion

Energieversorgung einer Zelle

Glycogenolyse

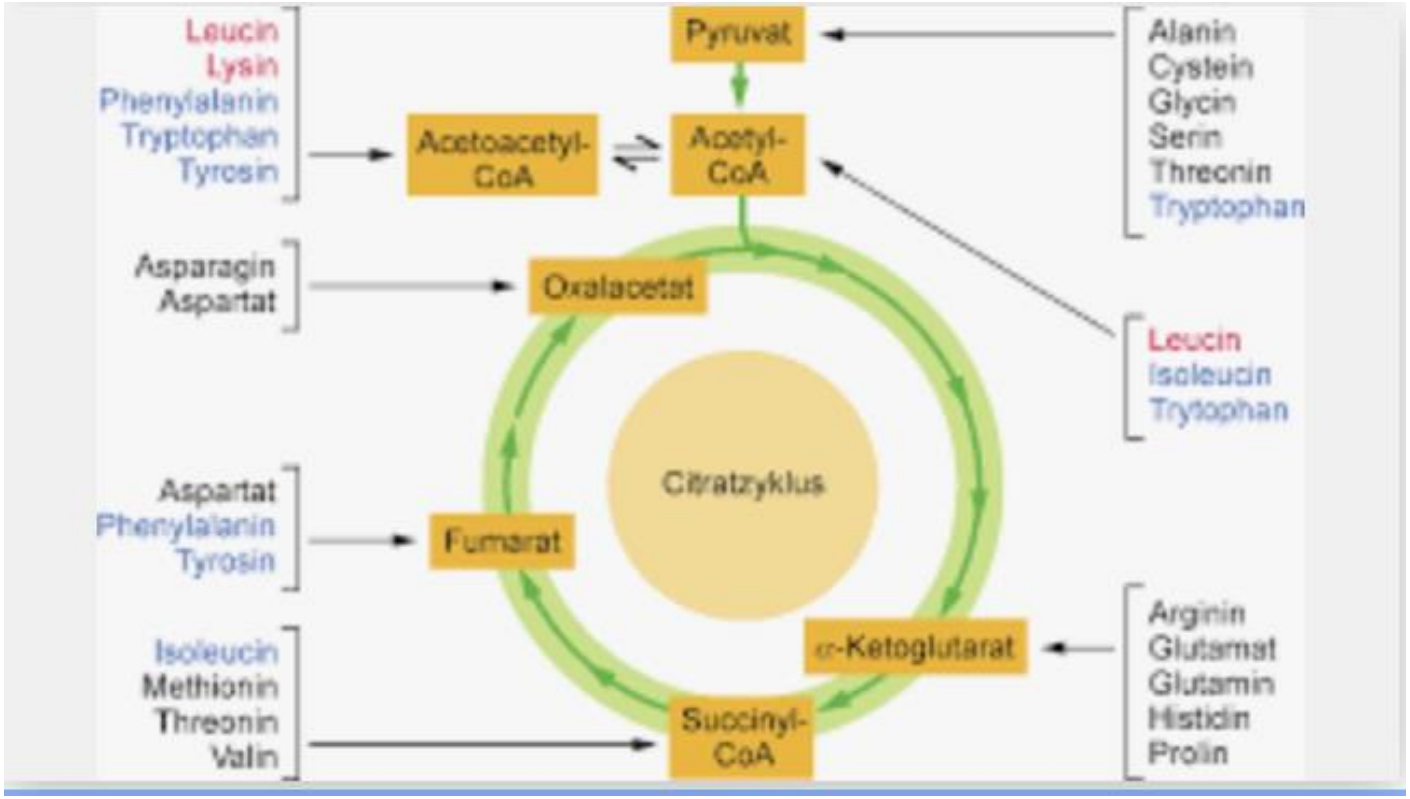




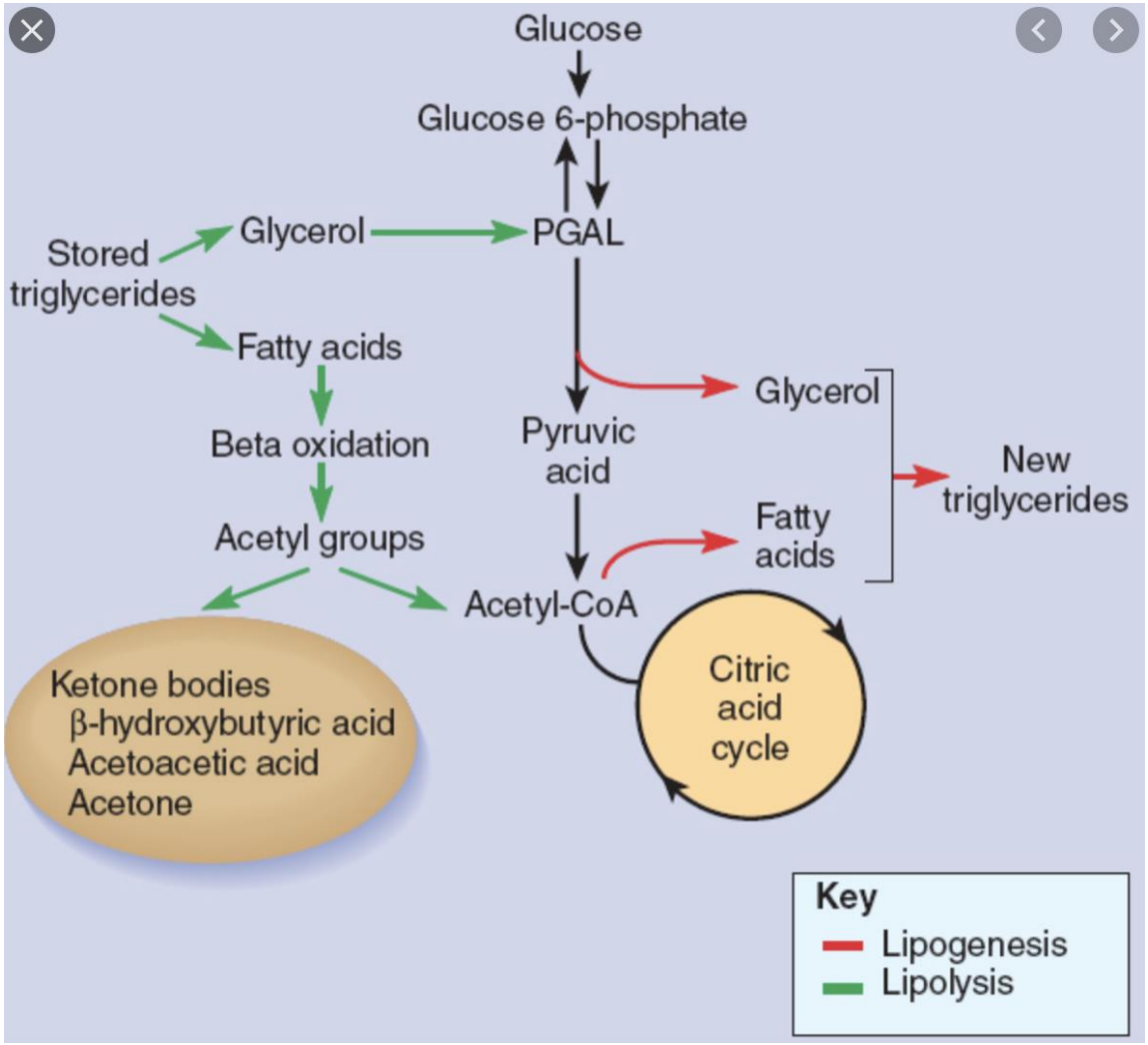


Glykogenspeicher = 12-24h

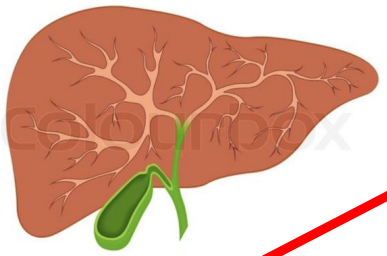
Proteinolyse

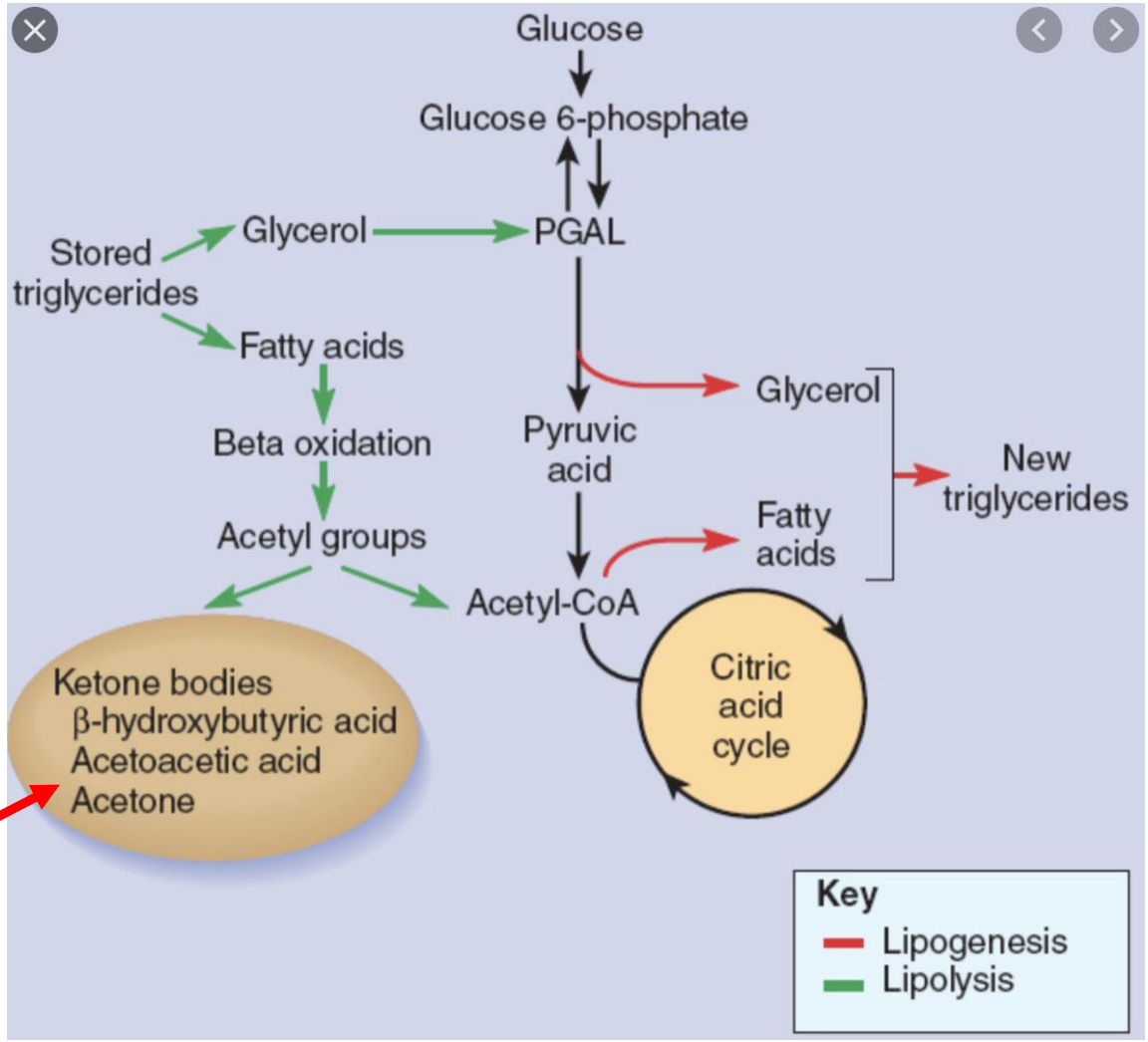


Lipolyse


Glucose
Glucose 6-phosphate
Stored triglycerides
Glycerol
PGAL
Fatty acids
Beta oxidation
Acetyl groups
Pyruvic acid
Glycerol
Fatty acids
New triglycerides
Acetyl-CoA
Citric acid cycle
Ketone bodies
β-hydroxybutyric acid
Acetoacetic acid
Acetone
Key
Lipogenesis
Lipolysis

Lipolyse




Glucose
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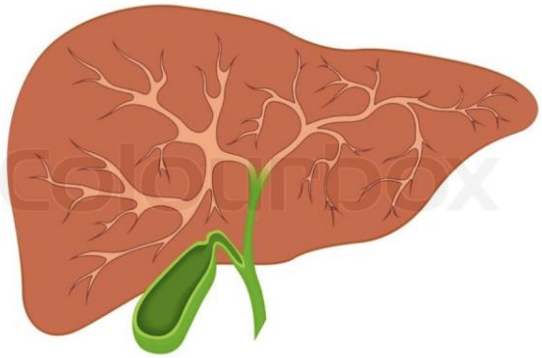
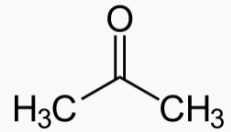
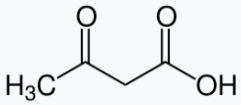
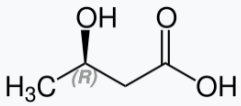
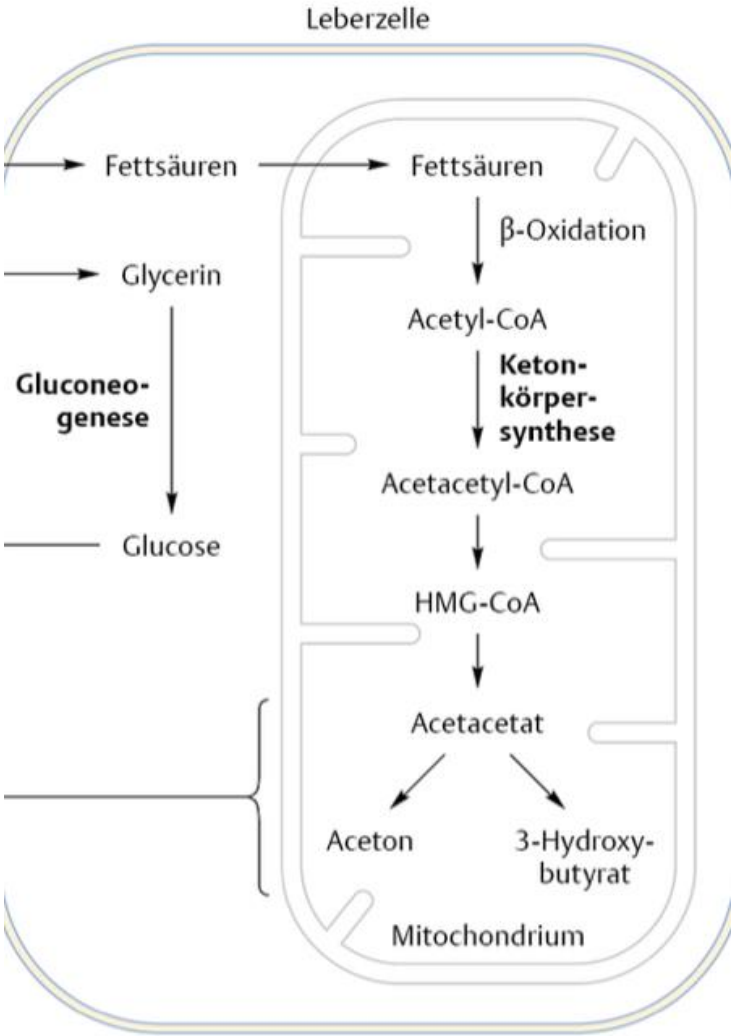
Citric acid cycle
Ketone bodies
β-hydroxybutyric acid
Acetoacetic acid
Acetone
Key
Lipogenesis
Lipolysis

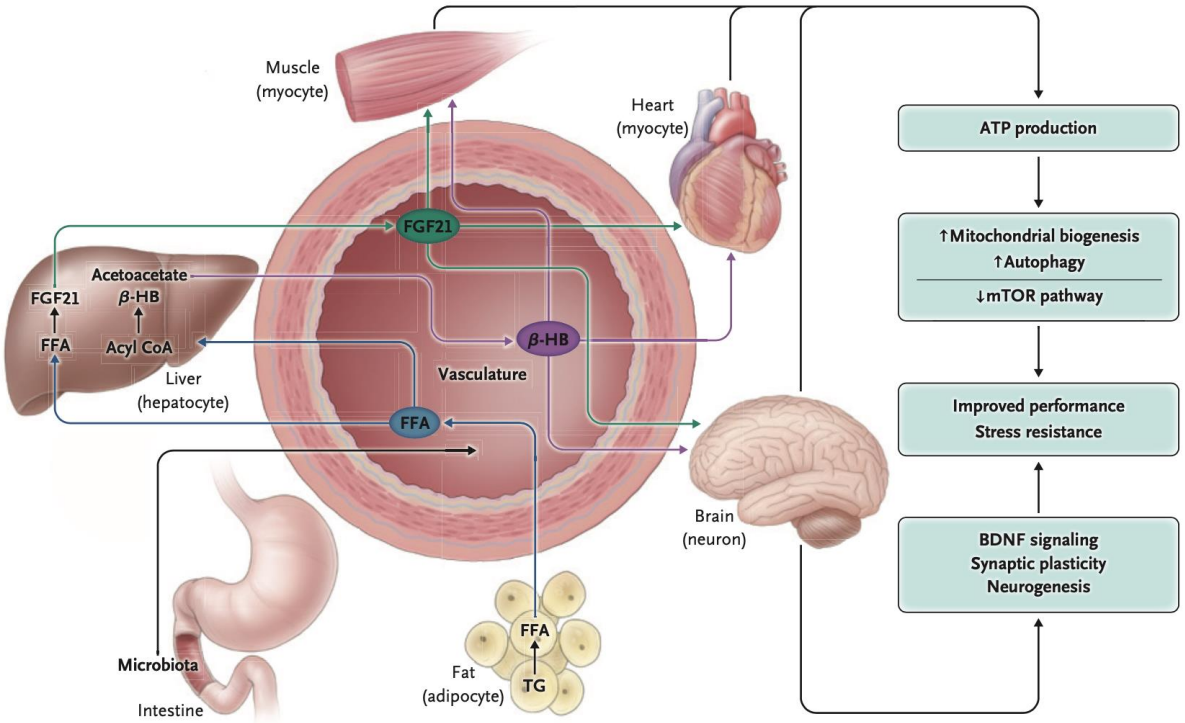
Ketonkörper = Glucose-Ersatz

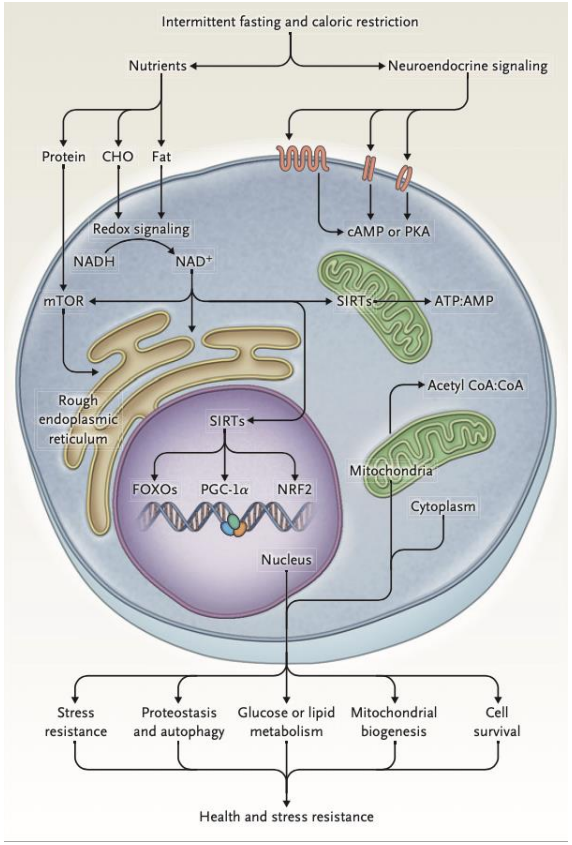


Ketokörper (Beispiele)
 Aceton
 3-Ketobuttersäure
 (*R*)-3-Hydroxybuttersäure β-Hydroxybuttersäure



Ketonkörper auch Transkriptionsfaktoren



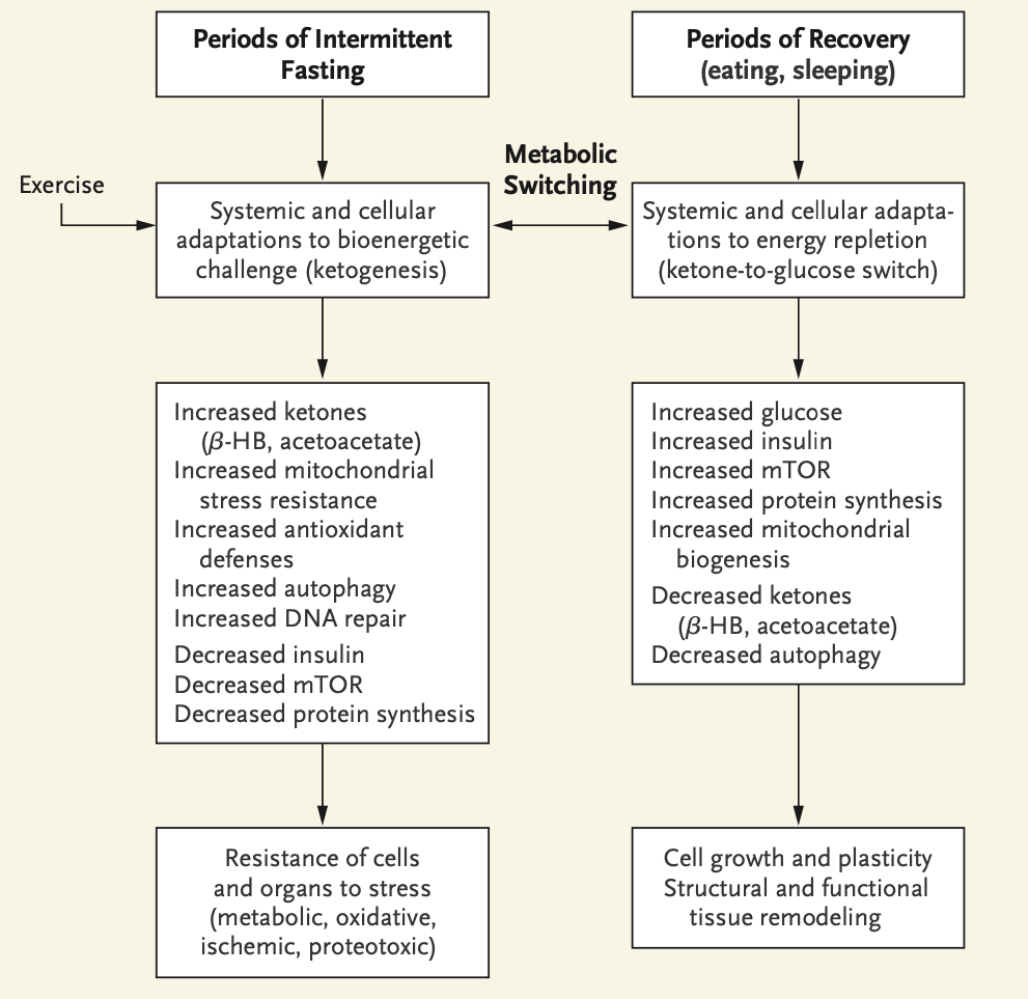


FGF21 = Fibroblast growth factor 21

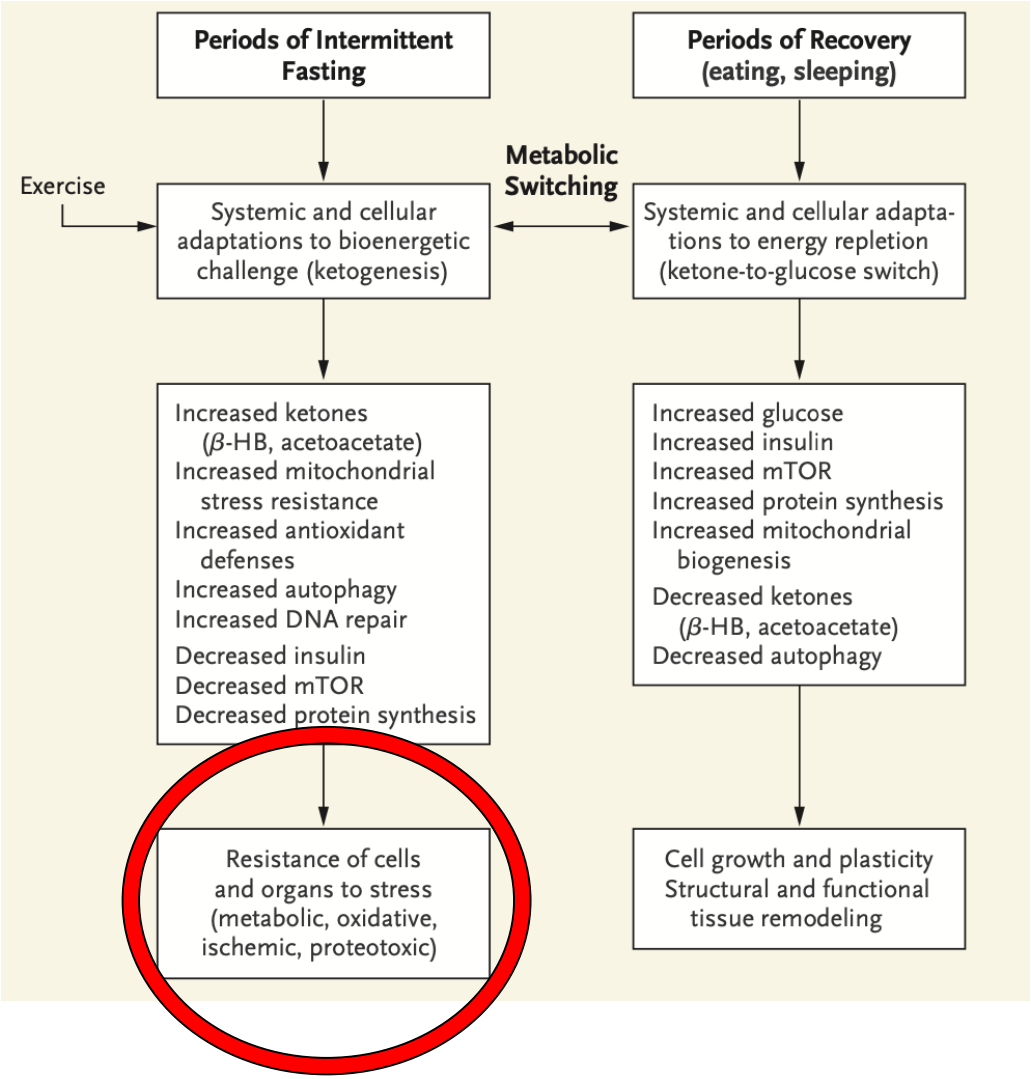
β-HB = Beta-Hydroxybutyrat

} Transkriptionsfaktoren

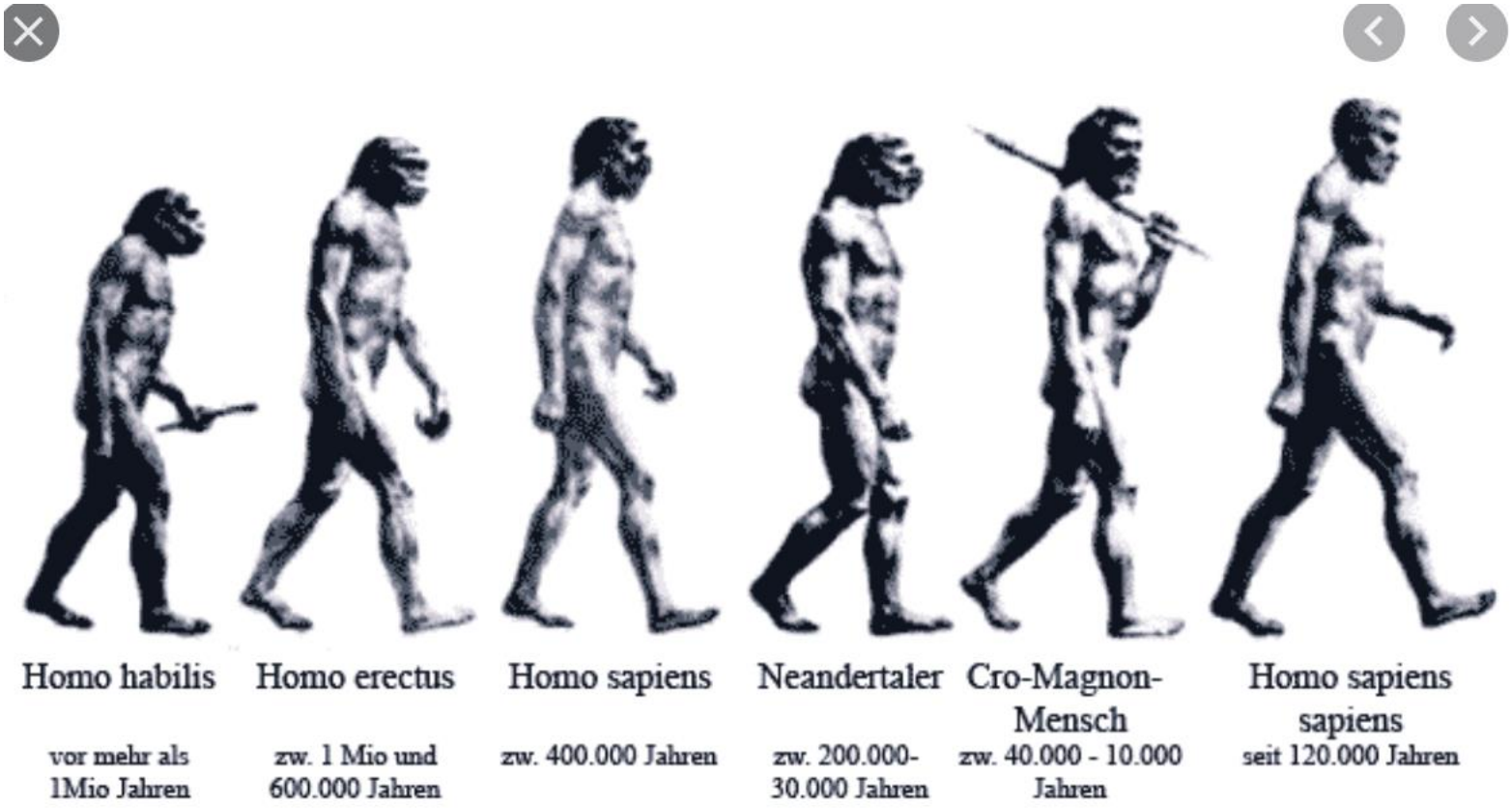
Zelluläre Mechanismen: Nahrungsabhängig



Zelluläre Mechanismen: Nahrungsabhängig



Evolution des Homo sapiens sapiens



Während Evolution: Lange Hungerperioden an der Tagesordnung
Optimale Anpassung des Körpers an Hungerperioden

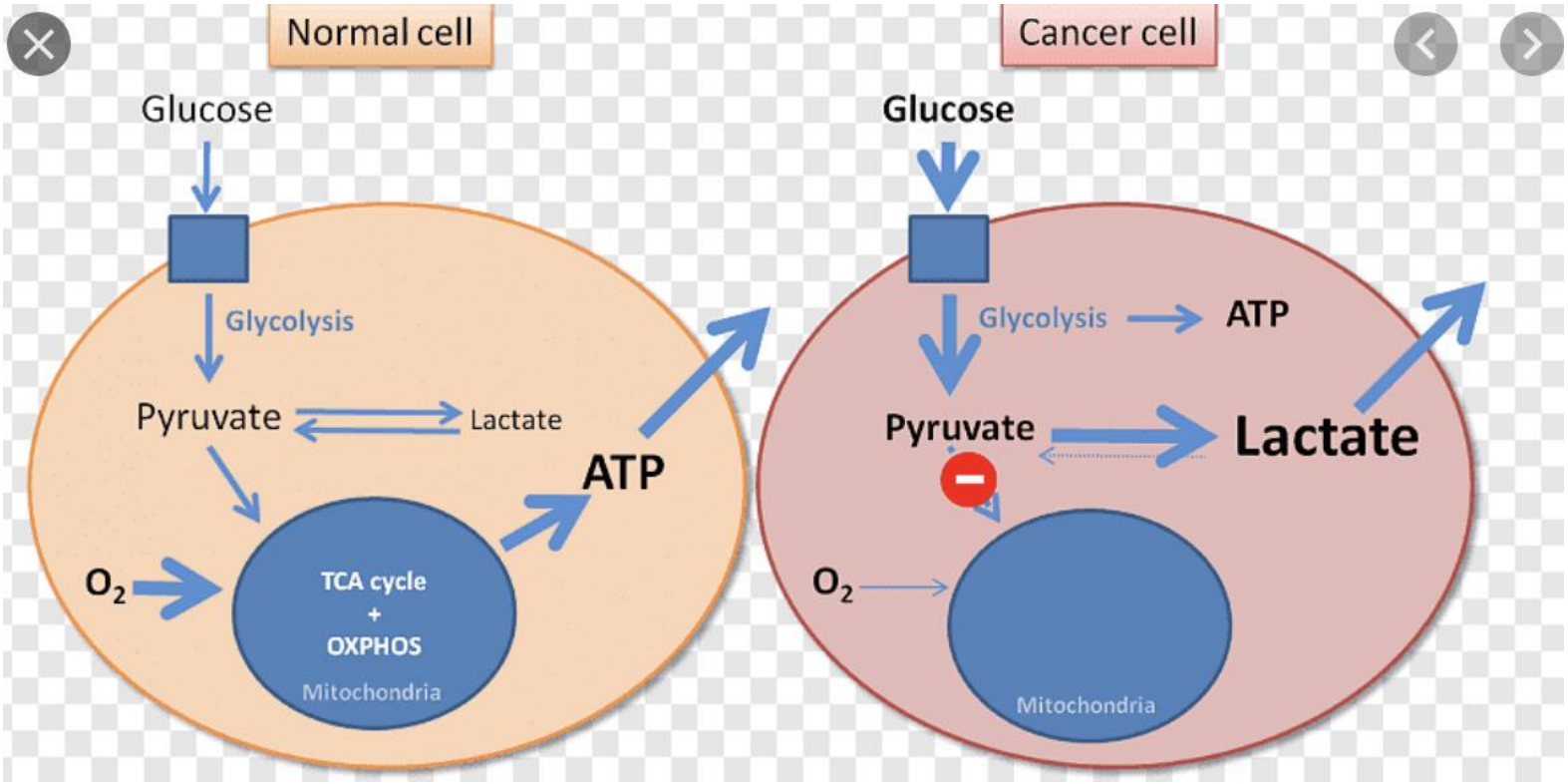
«Gesunde» Zelle versus «Tumorzelle»

«Gesunde» Zelle versus «Tumorzelle»

2 wichtige Differenzen bezüglich Metabolismus:

- Glucoseverbrauch
- Stressresistenz

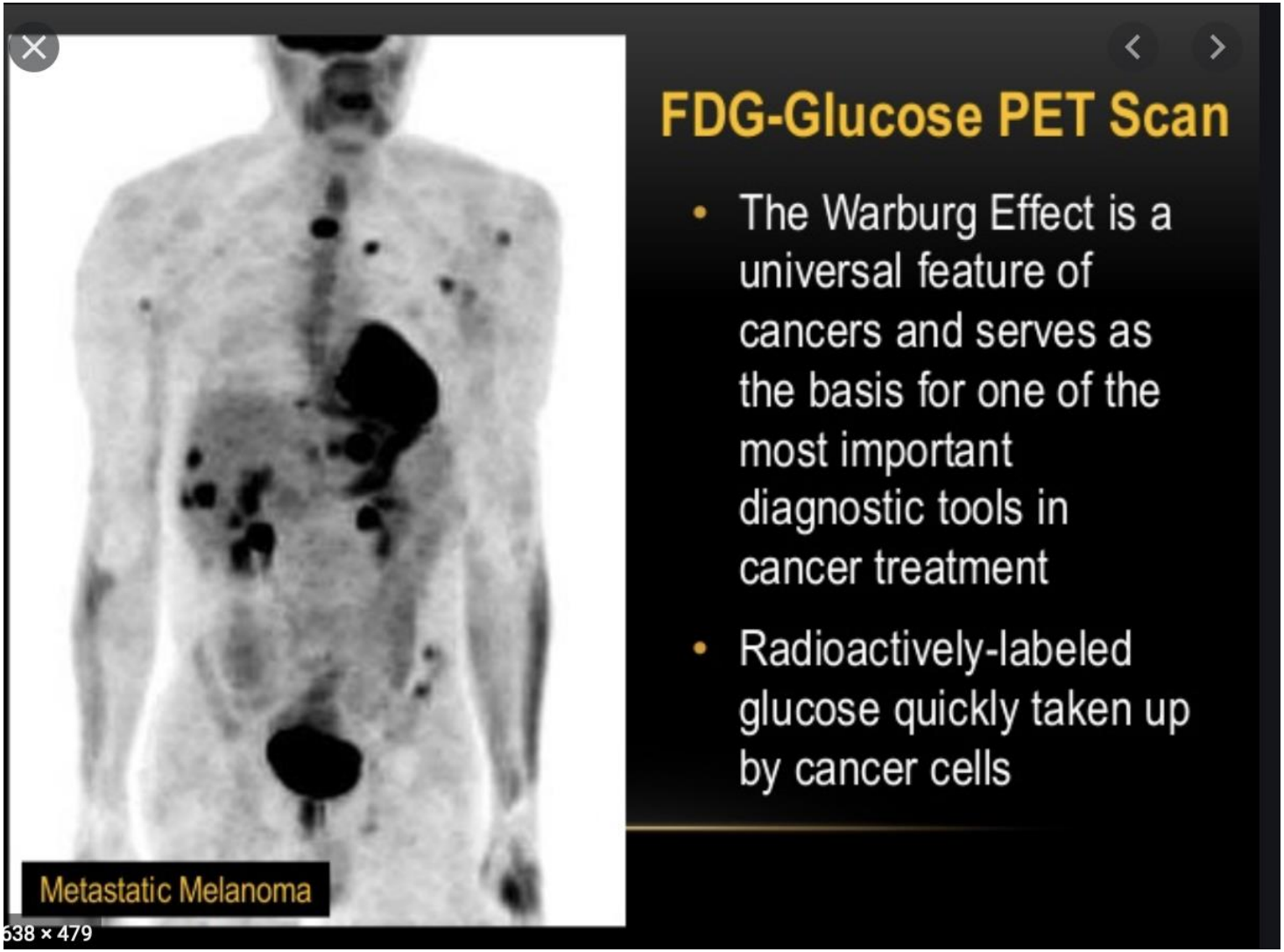
Glucoseverbrauch



36 mol ATP / mol Glucose

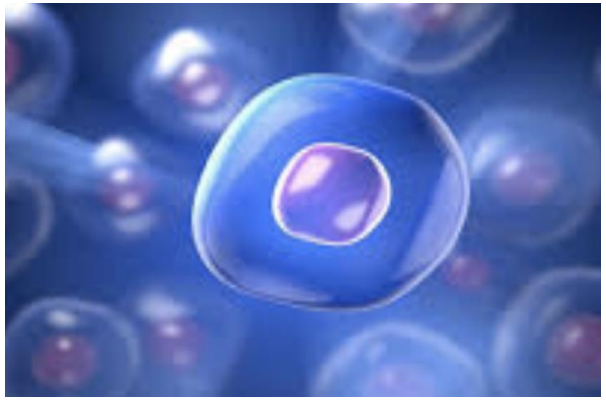
2 mol ATP / mol Glucose

«Warburg effect»

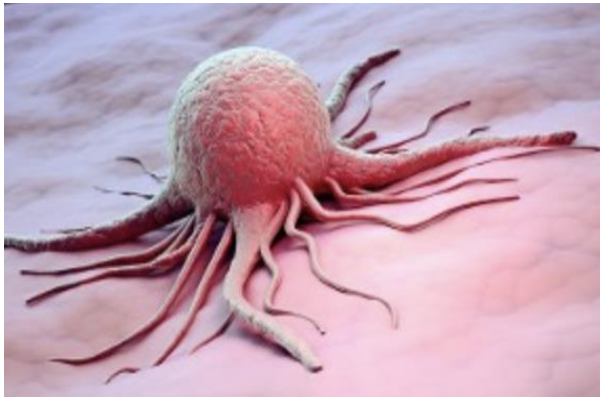


Stressresistenz

Stressresistenz

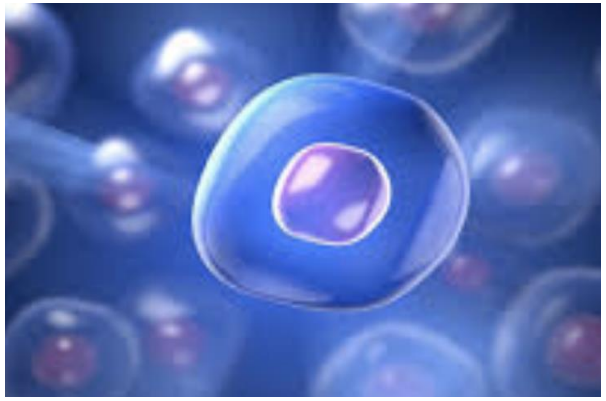


Adaption ↑



Wachstum ↑

Gesunde Zelle versus Krebszelle



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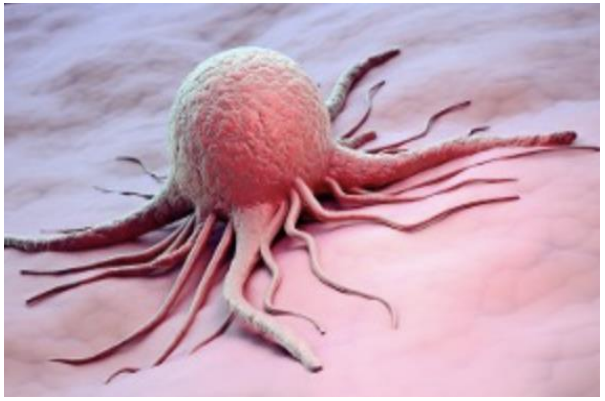

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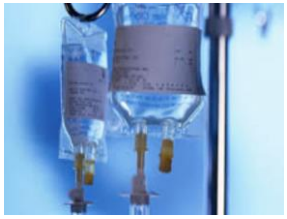
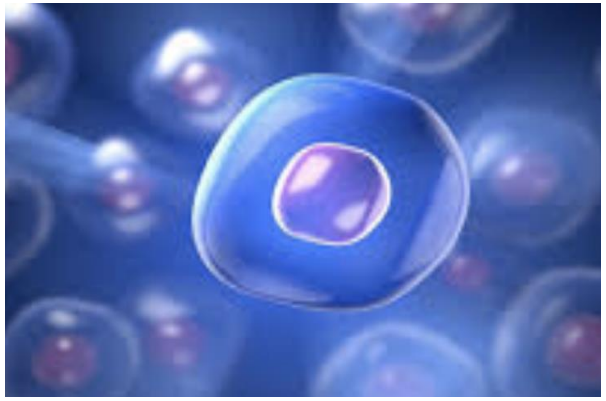
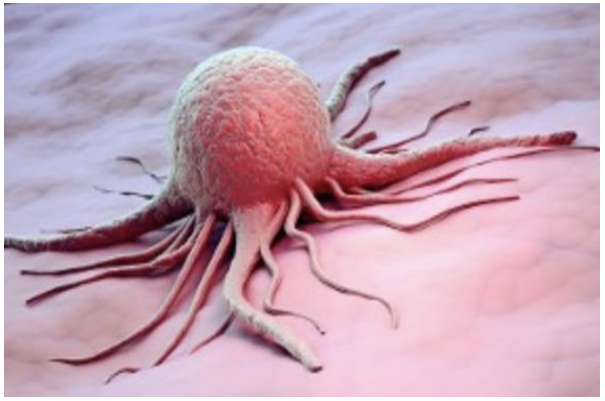


Gesunde Zelle versus Krebszelle





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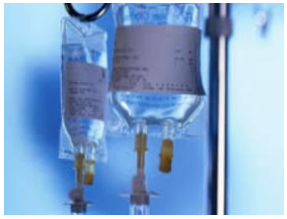
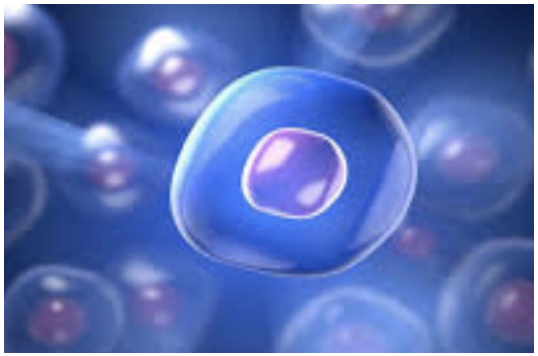
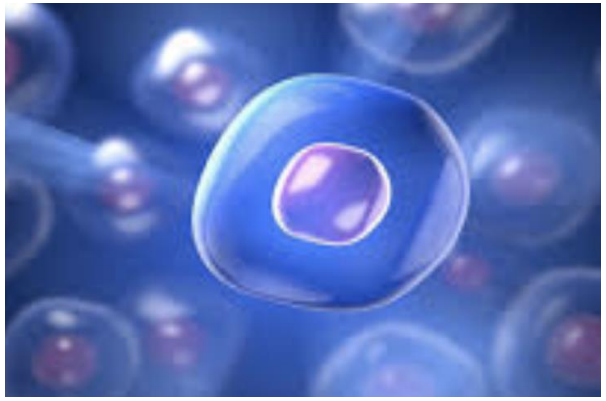
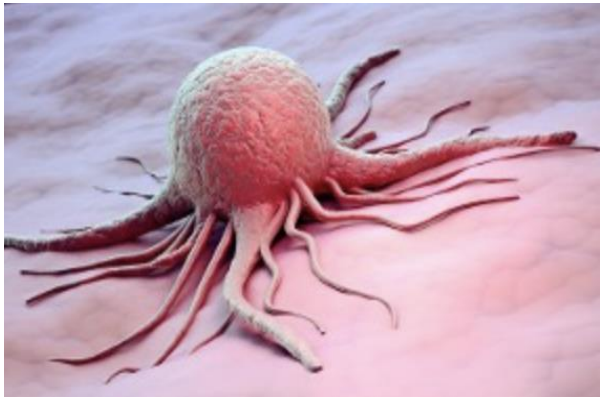




Gesunde Zelle versus Krebszelle





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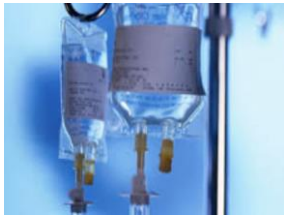
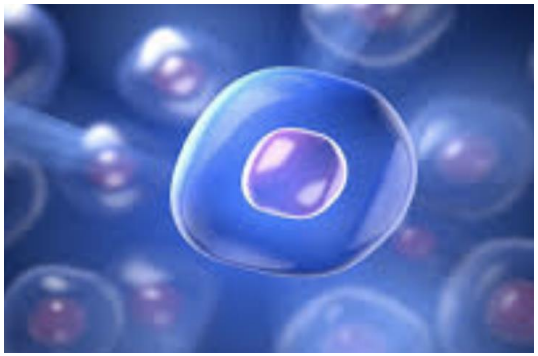
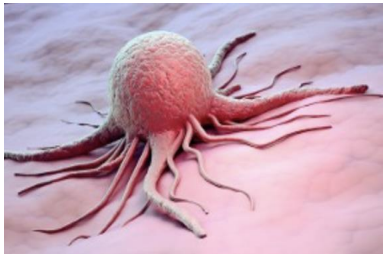
Wachstum ↑







Effekt des Fastens

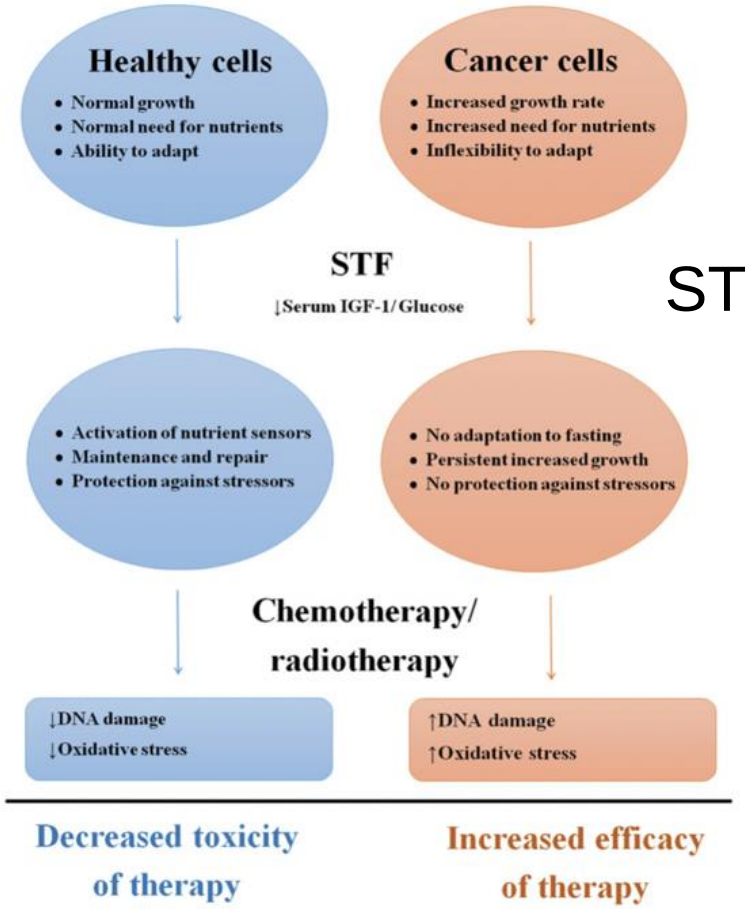


Fig. 1 Schematic overview of differential effects of short-term fasting on healthy and cancer cells. Abbreviations: STF; short term fasting, IGF-1: insulin growth factor-1.

STF=Short Term Fasting

Effekt des Fastens

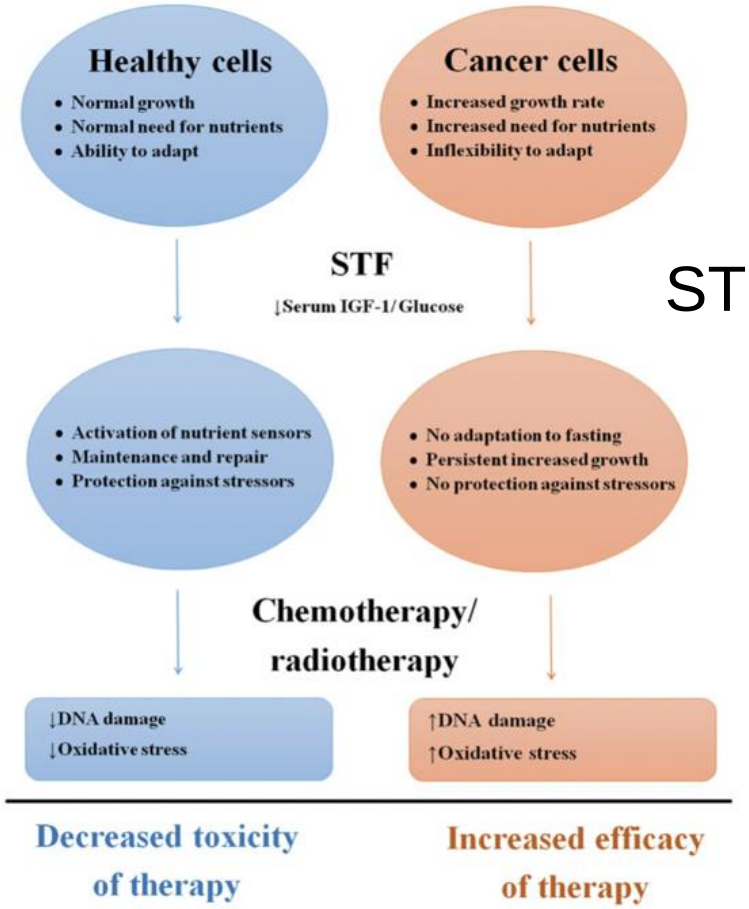
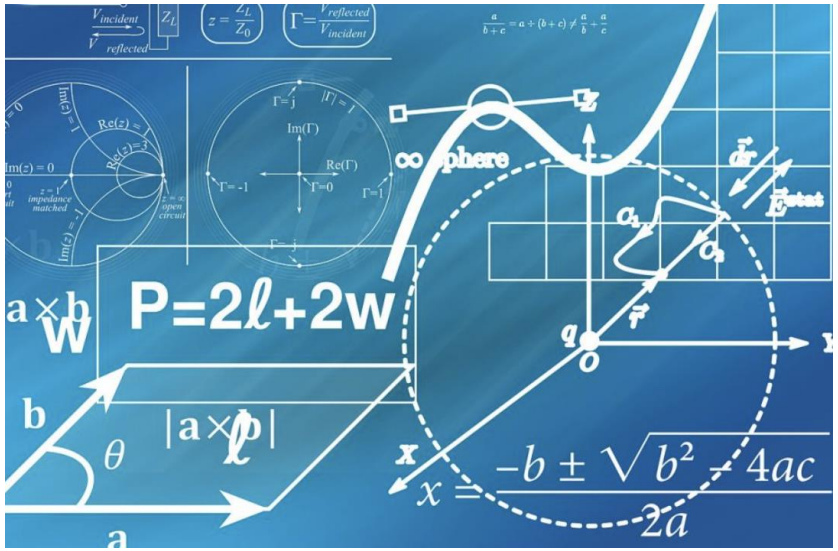


Fig. 1 Schematic overview of differential effects of short-term fasting on healthy and cancer cells. Abbreviations: STF; short term fasting, IGF-1: insulin growth factor-1.

STF=Short Term Fasting

Differential Stress Resistance

Energieversorgung einer Zelle



Effekt des Fastens im Tierversuch

Tierexperiment: Kal-Zufuhr-Lebensdauer

Tierexperiment: Kal-Zufuhr-Lebensdauer

1 Monat n. Geburt 12 Monat n. Geburt

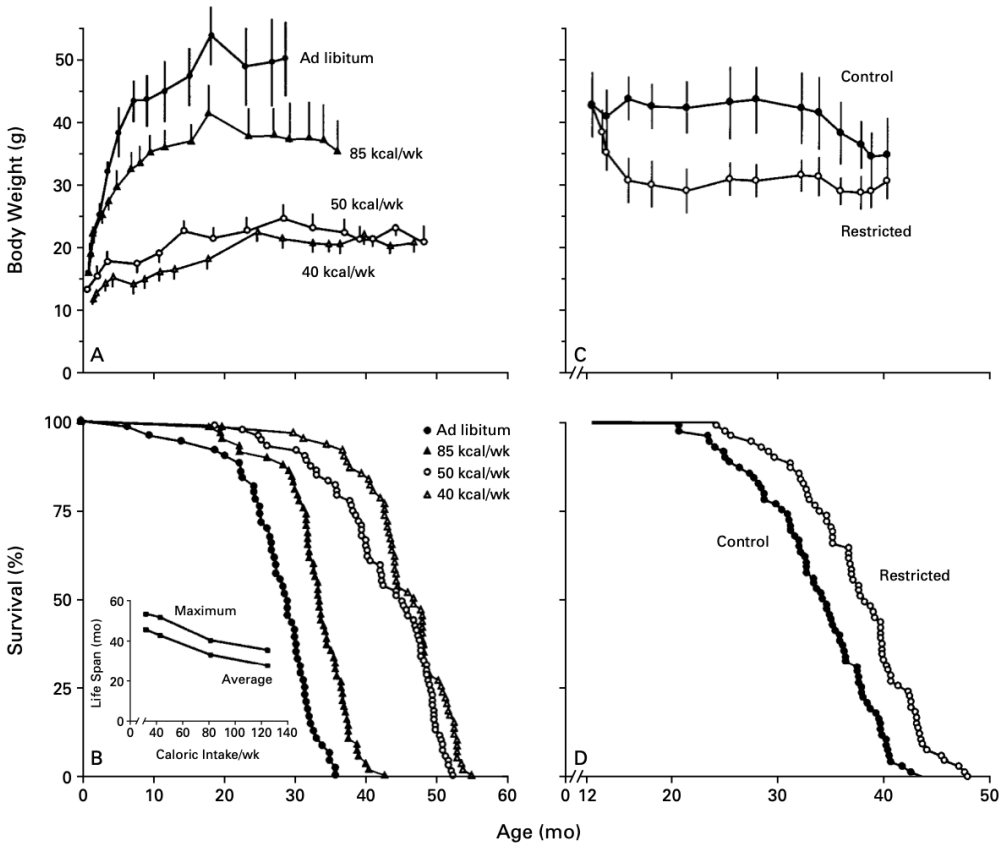
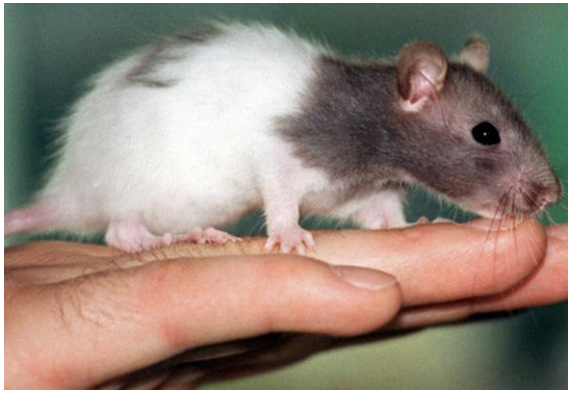


Figure 1. Effect of Caloric Restriction, Initiated at 1 Month or 12 Months of Age, on Body Weight and Life Span in Mice.

Tierexperiment: Kal-Zufuhr-Lebensdauer



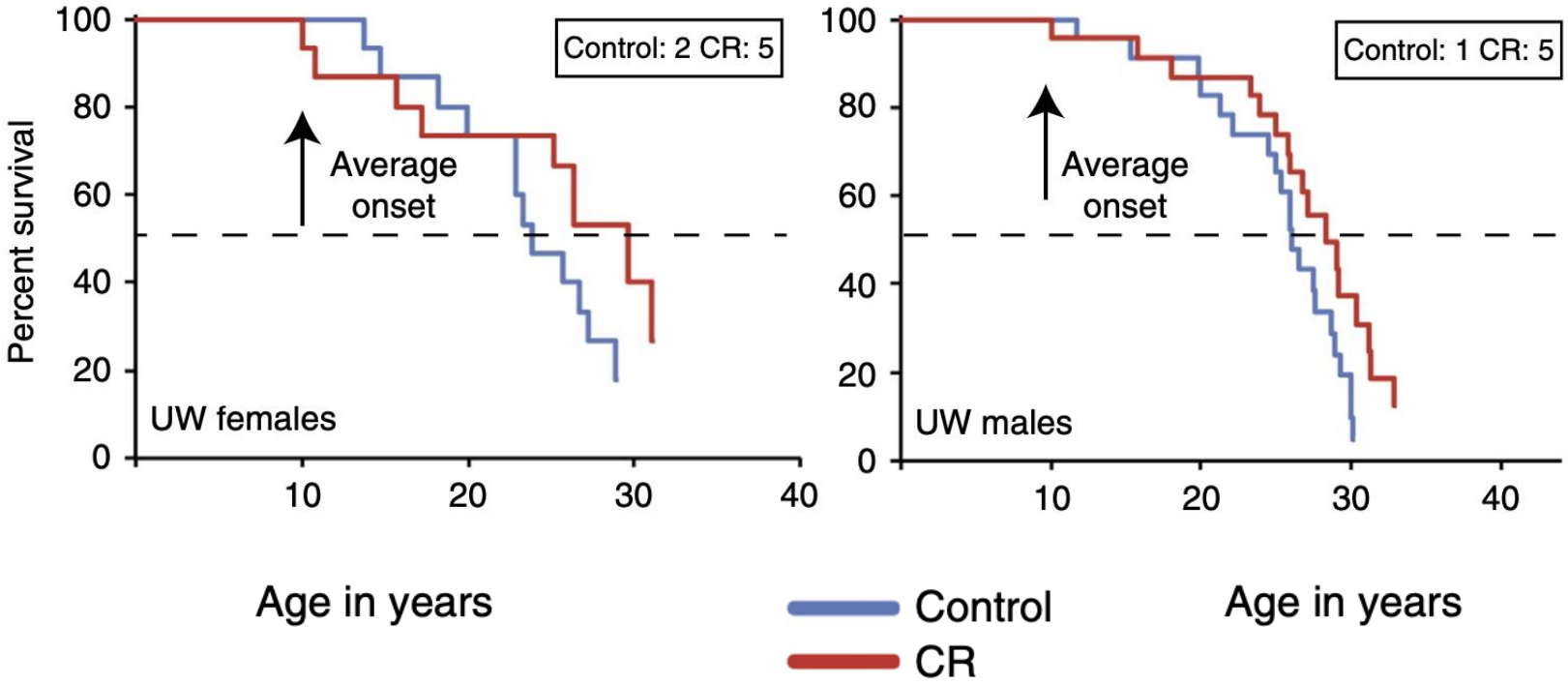
Metaanalyse von Rattenexperimenten

Supplemental Table 1. Laboratory experiments that have evaluated the effects of dietary restriction protocols on the survival of rats. The table lists 53 experiments involving a group of DR-fed rats paired with a reference group of rats maintained on a control diet (e.g., *ad lib* feeding). Experiments have been ordered chronologically according to the date of publication. Median and maximum lifespan estimates were reported in original research papers, or were otherwise estimated from published survival curves. In most cases, the median lifespan estimate is listed in the table (see "Median LS" columns and footnotes). Estimates listed under the "Max LS" columns correspond to one of several metrics, depending upon data reported in the published study (e.g., maximum survival time, average of longest-lived 10%; see footnotes).

Study	Strain	Sex	Sample Size (n)		Median LS (Months)		Max LS (Months)	
			DR	Control	DR	Control	DR	Control
McCay et al 1935[1]	White	M	13	14	26.6	17.4	42.8[d]	23.4[d]
McCay et al 1935[1]	White	F	23	22	30.1	27.4	41.8[d]	35.7[d]
McCay et al 1943[2]	White	M	10	19	36.2[†]	19.8[†]	39.7[b]	30.8[b]
McCay et al 1943[2]	White	F	10	19	37.5[†]	24.1[†]	41.6[b]	37.0[b]
Carlson and Hoelzel 1946[3]	Wistar	M	15	14	22.8[†]	20.4[†]	35.2[a]	27.0[a]
Carlson and Hoelzel 1946[3]	Wistar	F	15	19	24.4[†]	22.9[†]	35.3[a]	33.7[a]
Gilbert et al 1958[4]	Wistar	M	13	237	28.1	24.7	38.1[d]	32.3[d]
Gilbert et al 1958[4]	Wistar	F	14	349	30.0	23.1	39.1[d]	30.5[d]
Berg and Simms 1961[5]	Sprague-Dawley	M	79	89	33.3	25.0	38.3[a]	31.7[a]
Berg and Simms 1961[5]	Sprague-Dawley	F	39	79	> 40.0	30.3	> 40.0[a]	38.3[a]
Ross 1961[6]	Sprague-Dawley	M	210	25	31.3	10.2	44.4[a]	11.6[a]
Ross 1961[6]	Sprague-Dawley	M	120	25	33.0	22.7	49.3[a]	27.0[a]
Ross 1961[6]	Sprague-Dawley	M	210	25	29.3	30.3	42.9[a]	41.7[a]
Ross 1961[6]	Sprague-Dawley	M	195	25	33.0	21.7	54.6[a]	29.8[a]
Kibler and Johnson 1966[7]	Holzman	M	20	40	24.3[†]	19.6[†]	28.1[d]	23.6[d]

Tierversuch: Kal-Zufuhr-Lebensdauer

Affenexperiment: University of Wisconsin



nature COMMUNICATIONS

ARTICLE

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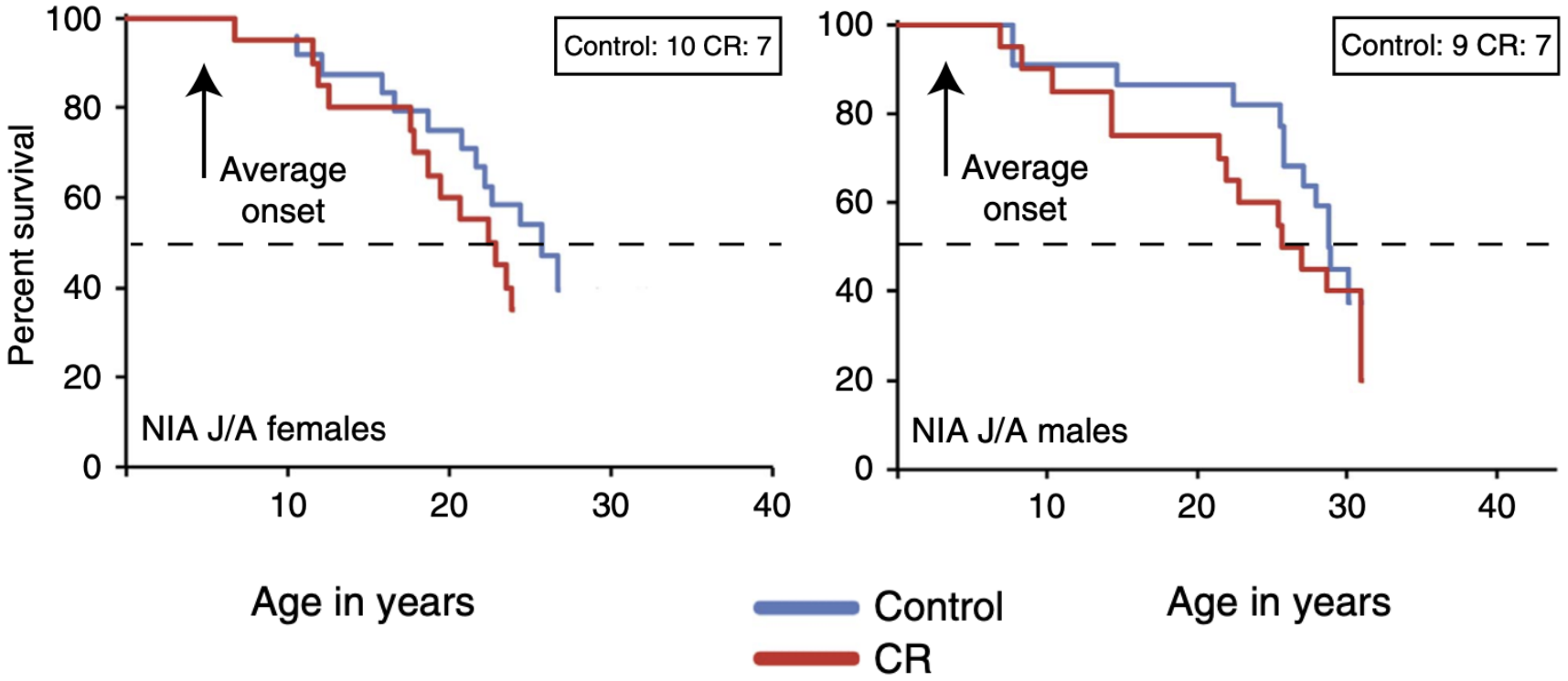
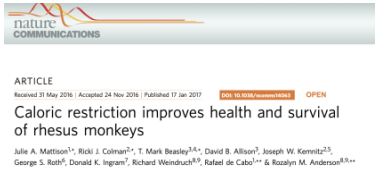
Caloric restriction improves health and survival of rhesus monkeys

Julie A. Mattison[1,*], Ricki J. Colman[2,*], T. Mark Beasley[3,4,*], David B. Allison[3], Joseph W. Kemnitz[2,5], George S. Roth[6], Donald K. Ingram[7], Richard Weindruch[8,9], Rafael de Cabo[1,*] & Rozalyn M. Anderson[8,9,**]

Affenexperiment: National Institute of Aging

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Gründe für lebensverlängernden Effekt

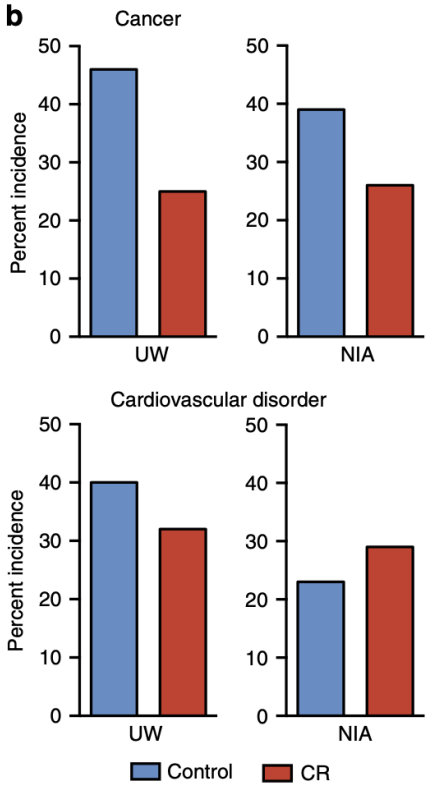


Figure 6 | Morbidity curves for monkeys at NIA and UW shown. (**a**) Graphs represent the first occurrence of any age-related disease, disorder or condition for combined males and females from UW (top) and NIA J/A (bottom). Statistics related to this figure are provided in Supplementary Information, Supplementary Table 4. (**b**) Incidence of prevalent age-related conditions in nonhuman primates for control and CR animals from UW and NIA (J/A and old-onset combined). To compare studies, cancer and cardiovascular disorders are reported as incidence upon necropsy and are expressed as a percentage of the animals that are deceased.

Effekt der Kalorienzufuhr im Tierversuch

- Übermässige Kalorienzufuhr hat lebensverkürzenden Effekt (Cave: minimale Kalorienzufuhr dringend notwendig!)
- Unklar, ob wir damit den Effekt des Fasten oder der fehlenden Gewichtszunahme studieren
- Alterserkrankungen wie Myokardinfarkt, CVI und Krebs können durch Kalorienrestriktion hinausgezögert bzw. verringert werden

Effekt des Fastens auf den Tumor im Tierversuch

Studie 1

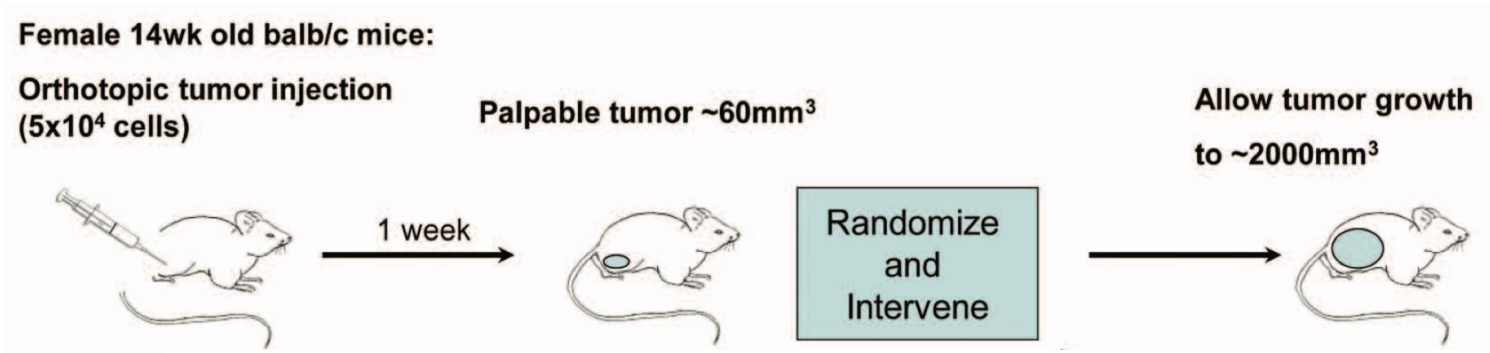
Cell Cycle 12:12, 1955–1963; June 15, 2013; © 2013 Landes Bioscience

Caloric restriction augments radiation efficacy in breast cancer

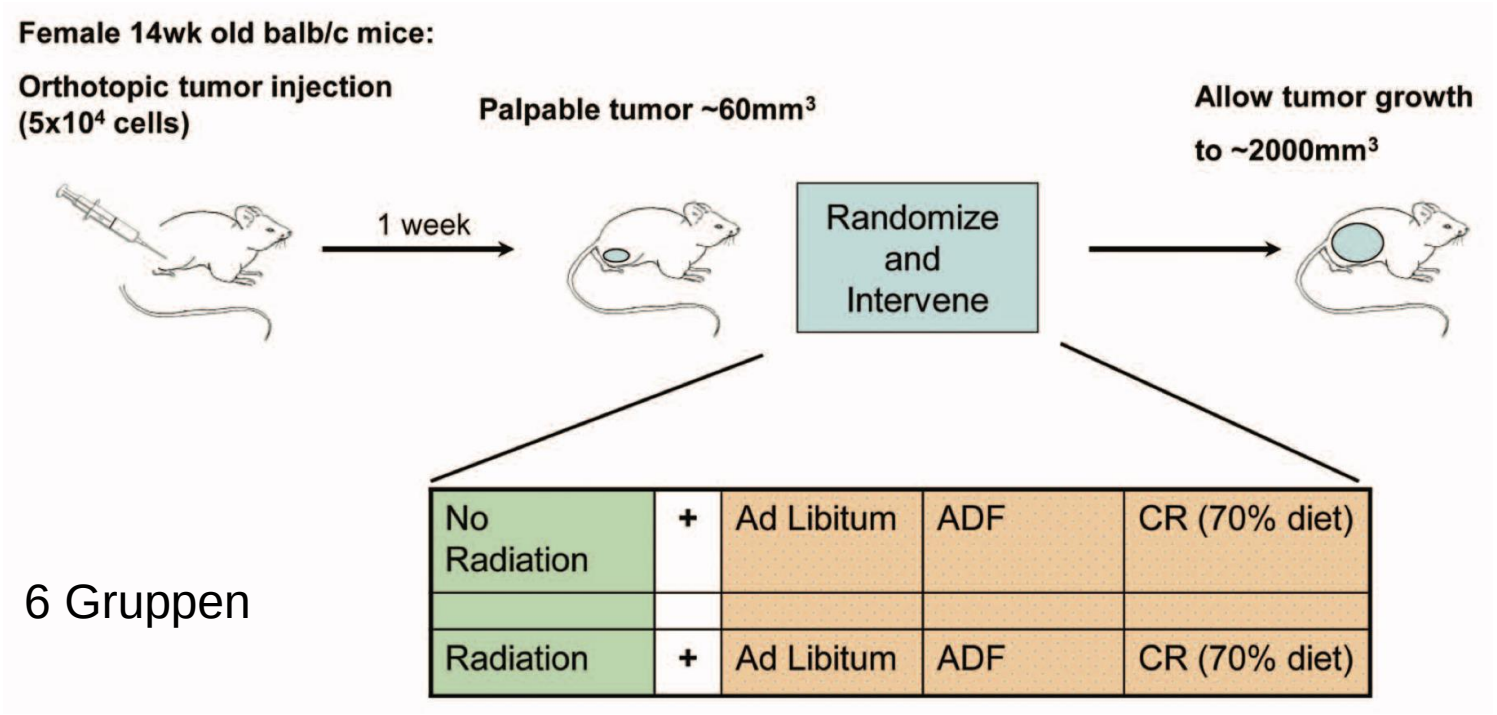
Anthony D. Saleh,[1] Brittany A. Simone,[2] Juan Palazzo,[3] Jason E. Savage,[1] Yuri Sano,[2] Tu Dan,[2] Lianjin Jin,[2] Colin E. Champ,[2] Shuping Zhao,[1] Meng Lim,[2] Frederica Sotgia,[4,†] Kevin Camphausen,[1] Richard G. Pestell,[4] James B. Mitchell,[5] Michael P. Lisanti[4,†] and Nicole L. Simone[2,*]

[1]Radiation Oncology Brach; National Cancer Institute; National Institutes of Health; Bethesda, MD USA; [2]Department of Radiation Oncology; Kimmel Cancer Center; Jefferson Medical College of Thomas Jefferson University; Philadelphia, PA USA; [3]Department of Pathology; Kimmel Cancer Center; Jefferson Medical College of Thomas Jefferson University; Philadelphia, PA USA; [4]Department of Cancer Biology; Kimmel Cancer Center; Thomas Jefferson University; Philadelphia, PA USA; [5]Radiation Biology Branch; National Cancer Institute; National Institutes of Health; Bethesda, MD USA

[†]Current affiliation: Manchester Breast Centre and Breakthrough Breast Cancer Research Unit; Paterson Institute for Cancer Research; Institute of Cancer Sciences; University of Manchester; Manchester, UK



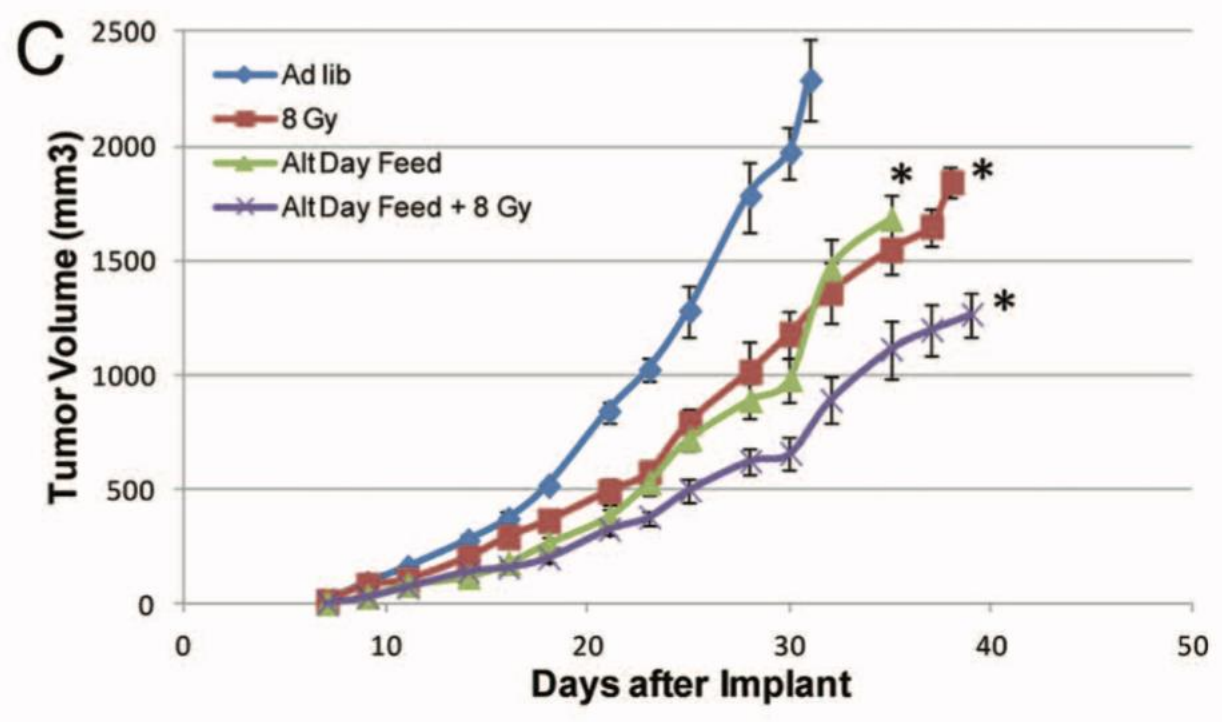
Studie 1



6 Gruppen

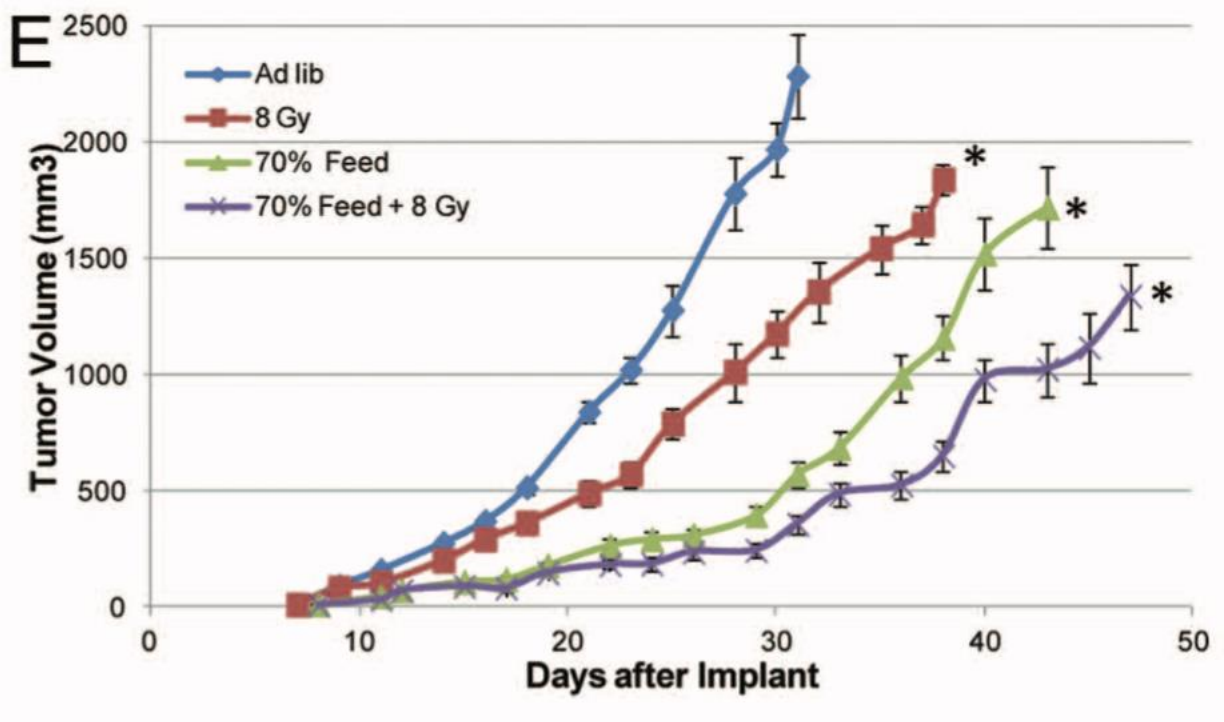
ADF = alternated day feeding
CR = Caloric restriction

Studie 1



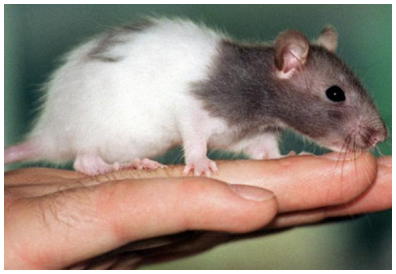
Ad libidum versus ADF +/- RT

Studie 1



Ad libidum versus 70% Feed +/- RT

Studie 2



Prostate Cancer and Prostatic Diseases (2010) 13, 350–355

1365-7852/10
www.nature.com/pcan

ORIGINAL ARTICLE

Effect of intermittent fasting on prostate cancer tumor growth in a mouse model

JA Thomas II[1], JA Antonelli[1], JC Lloyd[1], EM Masko[1], SH Poulton[1], TE Phillips[1], M Pollak[2] and SJ Freedland[1,3,4]

[1]*Division of Urologic Surgery, Department of Surgery, Duke Prostate Center, Duke University Medical Center, Durham, NC, USA;* [2]*Department of Oncology, Lady Davis Research Institute, McGill University, Montreal, Quebec, Canada;* [3]*Section of Surgery, Durham Veterans Administration Hospital, Durham, NC, USA and* [4]*Department of Pathology, Duke University Medical Center, Durham, NC, USA*

these findings in a larger study. A total of 100 (7- to 8-week-old) male severe combined immunodeficiency mice were injected subcutaneously with 1×10^5 LAPC-4 prostate cancer cells. Mice were randomized to either *ad libitum* Western Diet (44% carbohydrates, 40% fat and 16% protein) or *ad libitum* Western Diet with twice-weekly 24 h fasts (IF). Tumor volumes and mouse bodyweights were measured twice weekly. Mice were killed when tumor volumes reached 1000 mm^3. Serum and tumor were collected for analysis of the insulin/insulin-like growth factor 1

Studie 2

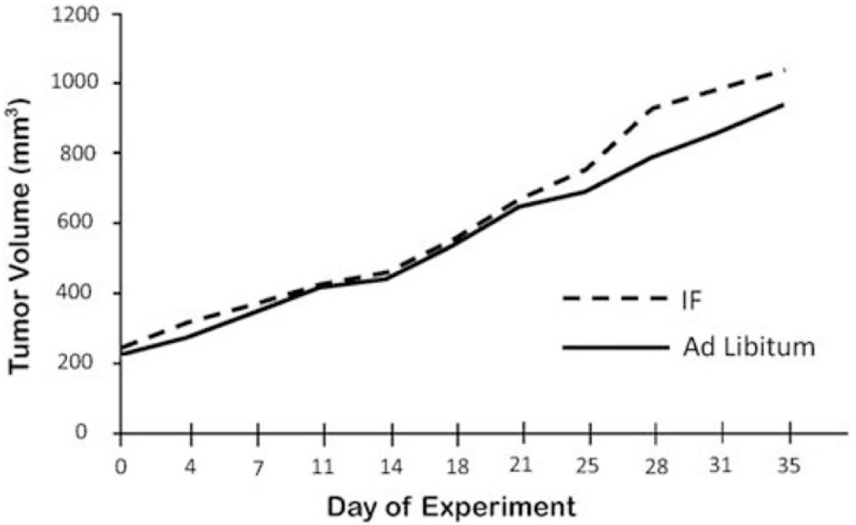


Figure 2 LAPC-4 xenograft tumor growth in severe combined immunodeficiency mice. Mice were injected subcutaneously with 1×10^5 LAPC-4 tumor cells. When tumors reached 200 mm^3 (day 0), mice were randomized to the two study arms. Tumor volumes were measured twice weekly. Values are expressed as median tumor volume of each group. Curves end on day 35, the median survival time for intermittent fasting (IF) mice.

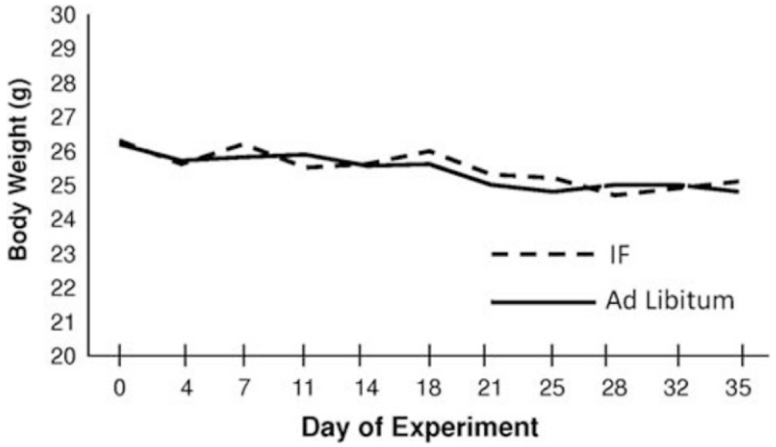
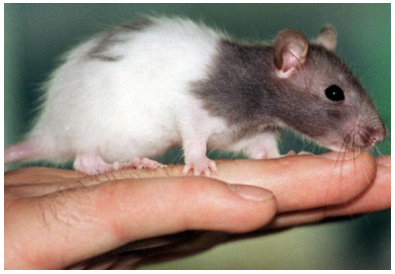


Figure 1 Mouse body weights. Mice were weighed twice weekly. Values expressed as median body weights over the course of the study for each group. IF, intermittent fasting.

Effekt der Fastens im Tierversuch

- Unterschiedliche Ergebnisse;



- tendenziell aber Benefit des Fastens bzgl Tumorwachstum in den Tierversuchen

Maus = Mensch ?

Studien beim Menschen zum Effekt des Short-Term-Fastings

de Groot *et al. Journal of Experimental & Clinical Cancer Research* (2019) 38:209
https://doi.org/10.1186/s13046-019-1189-9

Journal of Experimental & Clinical Cancer Research

REVIEW Open Access

Effects of short-term fasting on cancer treatment

Stefanie de Groot[1], Hanno Pijl[2], Jacobus J. M. van der Hoeven[1] and Judith R. Kroep[1*]

Table 2 Overview of clinical studies on the effect of STF on the toxicity of chemotherapy

Authors, site	Human Subjects	Treatment	Outcome
Safdie et al. 2009, USC, USA [136]	10 human subjects with distinct malignancies	Distinct + STF varying from 48 to 140 h prior and 5–56 h after CT	Safe and feasible. Reduction in CT-induced side effects.
Badar et al. 2014, KFMC, Saudi Arabia, NCT00757094 [135]	11 human subjects with distinct malignancies	IF during Ramadan when receiving CT	Safe and feasible. Reduction in CT-induced side effects[a].
Dorff et al. 2016, USC, USA, NCT00936364, [22, 137]	20 human subjects with distinct malignancies	Platinum based CT + 24 h, 48 h or 72 h STF	Safe and feasible . Reduces DNA damage in leukocytes (dose response). Reduction of IGF-1 (dose response).
de Groot et al. 2015, LUMC, The Netherlands NCT01304251 [131]	13 women with stage II and III HER2 negative breast cancer	TAC CT ± 48 h STF	Safe and feasible. Reduction in IGF-1 Beneficial effect on erythrocytes and thrombocytes Possible reduction in DNA damage in healthy cells
Bauersfeld et al. 2018, Charite University, Germany, NCT01954836 [138]	34 women with breast and ovarian cancer	CT ± 60 h STF (cross-over)	Safe and feasible Beneficial effect on QOL, fatigue and well-being

USC University of Southern California, *KFMC* King Fahad Medical City, *LUMC* Leiden University Medical Center, *UC Davis* University of California, Davis School of Veterinary Medicine, *STF* Short-term fasting, *IF* intermittent fasting, *CT* Chemotherapy, *TAC* docetaxel/doxorubicin/cyclophosphamide, *IGF-1* insulin-like growth factor-1, *QOL* Quality of life [a]no statistics performed

Studie 1

de Groot *et al. BMC Cancer* (2015) 15:652
DOI 10.1186/s12885-015-1663-5

BMC Cancer

RESEARCH ARTICLE Open Access

CrossMark

The effects of short-term fasting on tolerance to (neo) adjuvant chemotherapy in HER2-negative breast cancer patients: a randomized pilot study

Stefanie de Groot[1], Maaike PG Vreeswijk[2], Marij JP Welters[1], Gido Gravesteijn[2], Jan JWA Boei[2], Anouk Jochems[1], Daniel Houtsma[3], Hein Putter[4], Jacobus JM van der Hoeven[1], Johan WR Nortier[1], Hanno Pijl[5] and Judith R Kroep[1*]

- 13 Frauen mit Mamma-Ca, welche eine neo- oder adjuvante Chemotherapie mit TAC benötigten
- STF = 48h Fasten (24 vor und nach Chemotherapie): nur Wasser und Tee ohne Zucker; 7 Patientinnen
- Non-STF: gesunde Ernährung mit mind. 2 Fruchtstücken / d; 6 Patientinnen
- Primäre Fragestellung: Toxizität geringer unter SFT?

Non-Hämatologische NW

Table 2 Grade I/II and grade III/IV toxicity during 6 cycles of TAC in both groups

	Grade I/II	
	STF	Non-STF
Fatigue	5 (71 %)	6 (100 %)
Infection	3 (43 %)	1 (17 %)
Mucositis	4 (57 %)	4 (67 %)
Neuropathy	5 (71 %)	3 (50 %)
Diarrhea	5 (71 %)	2 (33 %)
Dizziness	3 (43 %)	3 (50 %)
Nausea	7 (100 %)	4 (67 %)
Eye complaints	4 (57 %)	2 (33 %)
Constipation	4 (57 %)	2 (33 %)
	Grade III/IV	
Total	6	3
Neutropenic fever	2 (29 %)	2 (33 %)
Fatigue	2 (29 %)	0 (0 %)
Infection	2 (29 %)	1 (17 %)

All side effects were scored according CTCAE4.03. Each side effect was scored maximal once per patient during the course (the highest grade of occurrence was scored)
STF short-term fasting

Cave: Nebenwirkungen wurden durch Patientinnen graduiert

Non-Hämatologische NW

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Infection	2 (29 %)	1 (17 %)

All side effects were scored according CTCAE4.03. Each side effect was scored maximal once per patient during the course (the highest grade of occurrence was scored)
STF short-term fasting

40 / 7= 571%

27 / 6= 450%

Cave: Nebenwirkungen wurden durch Patientinnen graduiert

Non-Hämatologische NW

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Fatigue	2 (29 %)	0 (0 %)
Infection	2 (29 %)	1 (17 %)

All side effects were scored according CTCAE4.03. Each side effect was scored maximal once per patient during the course (the highest grade of occurrence was scored)
STF short-term fasting

6 / 7= 85%

3 / 6= 50%

Cave: Nebenwirkungen wurden durch Patientinnen graduiert

Studie 2

nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-020-16138-3 OPEN

Check for updates

Fasting mimicking diet as an adjunct to neoadjuvant chemotherapy for breast cancer in the multicentre randomized phase 2 DIRECT trial

Stefanie de Groot[1], Rieneke T. Lugtenberg[1], Danielle Cohen[2], Marij J. P. Welters[1], Ilina Ehsan[1], Maaike P. G. Vreeswijk[3], Vincent T. H. B. M. Smit[2], Hiltje de Graaf[4], Joan B. Heijns[5], Johanneke E. A. Portielje[1,6], Agnes J. van de Wouw[7], Alex L. T. Imholz[8], Lonneke W. Kessels[8], Suzan Vrijaldenhoven[9], Arnold Baars[10], Elma Meershoek-Klein Kranenbarg[11], Marjolijn Duijm-de Carpentier[11], Hein Putter[12], Jacobus J. M. van der Hoeven[1], Johan W. R. Nortier[1], Valter D. Longo[13,14], Hanno Pijl[15], Judith R. Kroep[1✉] & Dutch Breast Cancer Research Group (BOOG)[16,*]

Studie 2

- Patientinnen mit lokalisertem Mammakarzinom vor neoadjuvanter CT
- Fasting mimicking diet (FMT) 3 Tag vor der CT sowie am Tag der CT (zubereitete Suppen, Brühen, Teas; d1: 1200kcal, d2-4: 200kcal)
- Kontrollgruppe: reguläre Diät ohne Kalorienrestriktion
- Randomisierte, observer-blinded Studie
- Primärer Endpunkt: - Grad III/IV Toxizitäten
  - pCR

Studie 2

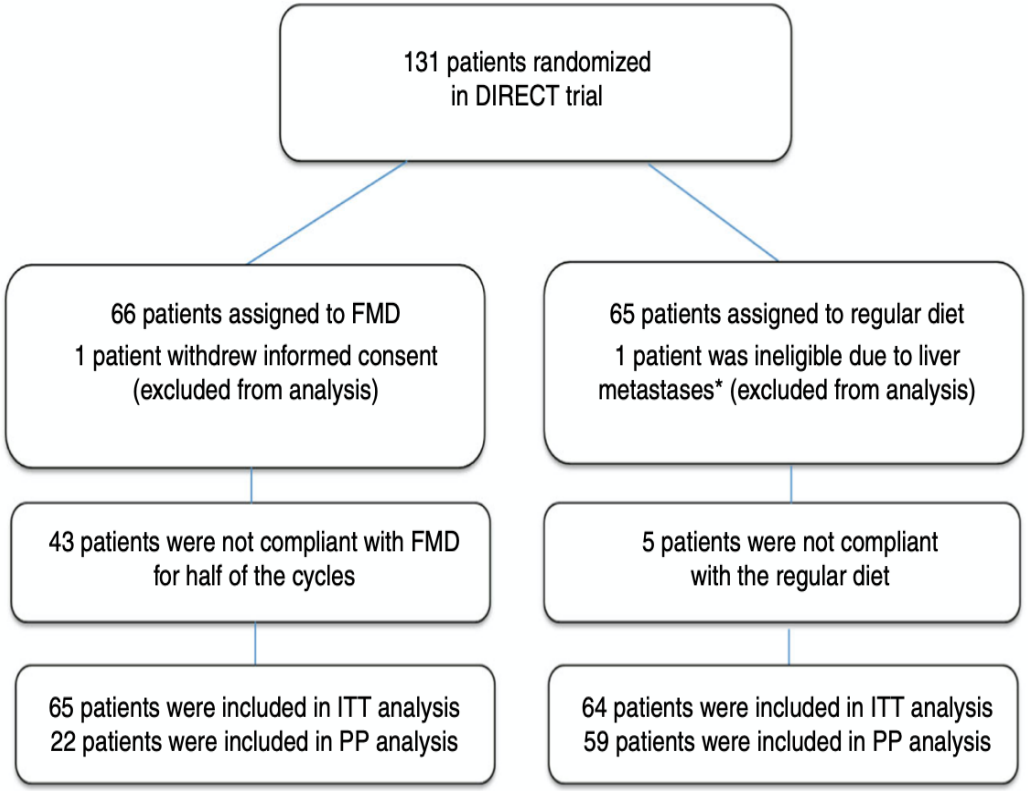


Fig. 1 Consort diagram of the DIRECT study. This figure shows reasons for exclusion from the study and the numbers of patients included in the PP and ITT analyses. Abbreviations: FMD: fasting mimicking diet, ITT: Intention to treat, PP: Per protocol. * diagnosed the day after randomization.

Studie 2 Grad III / IV Toxizität

Table 2 Grade III/IV toxicity in both groups (ITT) and in patients who were compliant with the FMD for at least half cycles of CT vs. control patients who did not fast on their own initiative (PP).

Grade III/IV	FMD (*N* = 65)	FMD-C (*N* = 22)	FMD-NC (*N* = 43)	Control (*N* = 64)	*P*-value (ITT)	*P*-value (PP)
Total	31 (47.7%)	11 (50.0%)	20 (46.5%)	36 (56.3%)	0.331	0.539
Neutropenic fever	5 (7.7%)	1 (4.5%)	4 (9.3%)	5 (7.8%)	0.980	0.548
Neutropenia	19 (29.2%)	6 (27.3%)	13 (30.2%)	18 (28.1%)	0.890	0.777

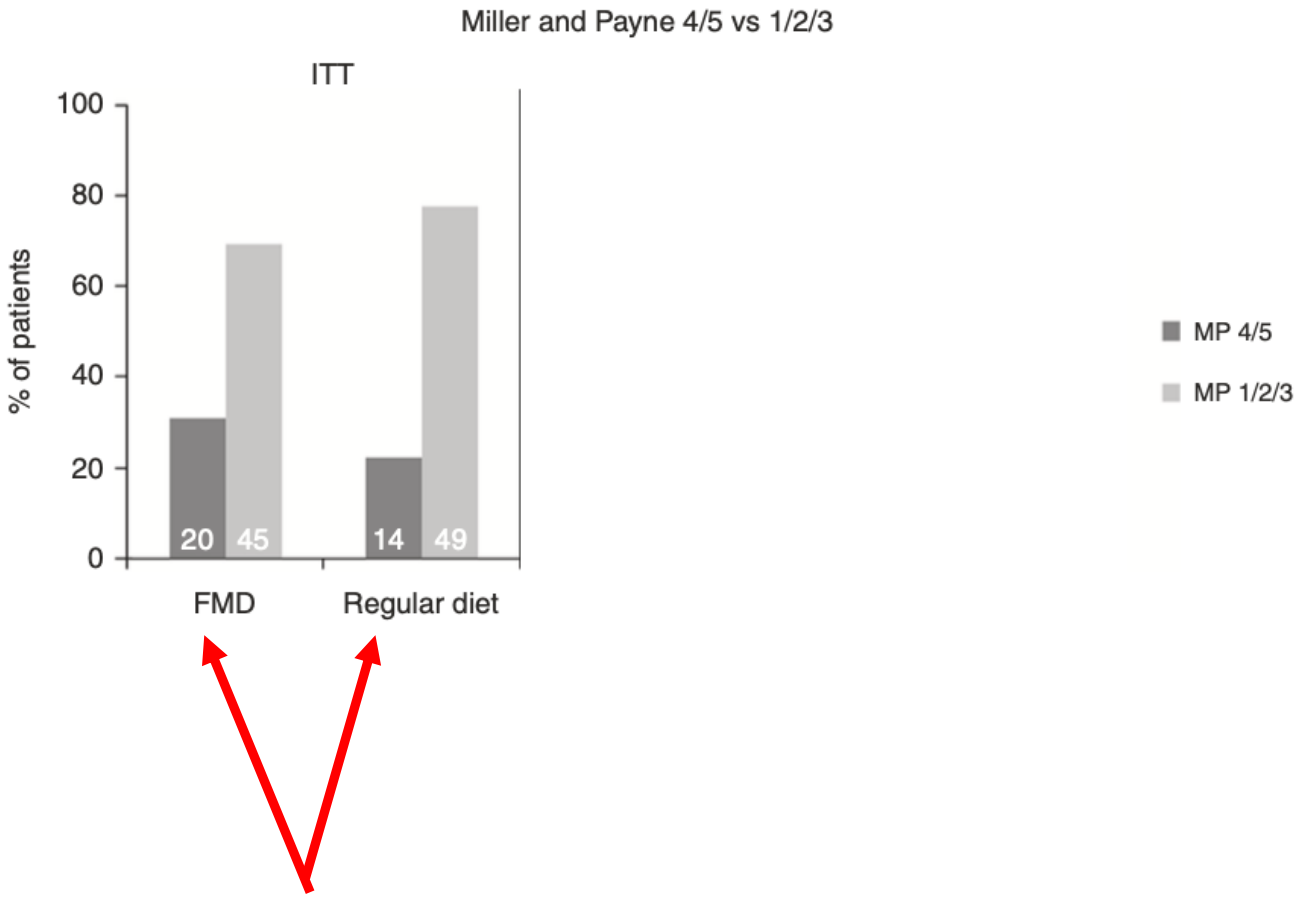
Grade III/IV side effects were scored according CTCAE4.03. Each side effect was scored maximal once per patient during the course. *FMD* fasting mimicking diet, *C* compliant, *NC* not compliant, *ITT* intention to treat, *PP* per protocol, *CT* chemotherapy.

Studie 2 Tumoransprechen

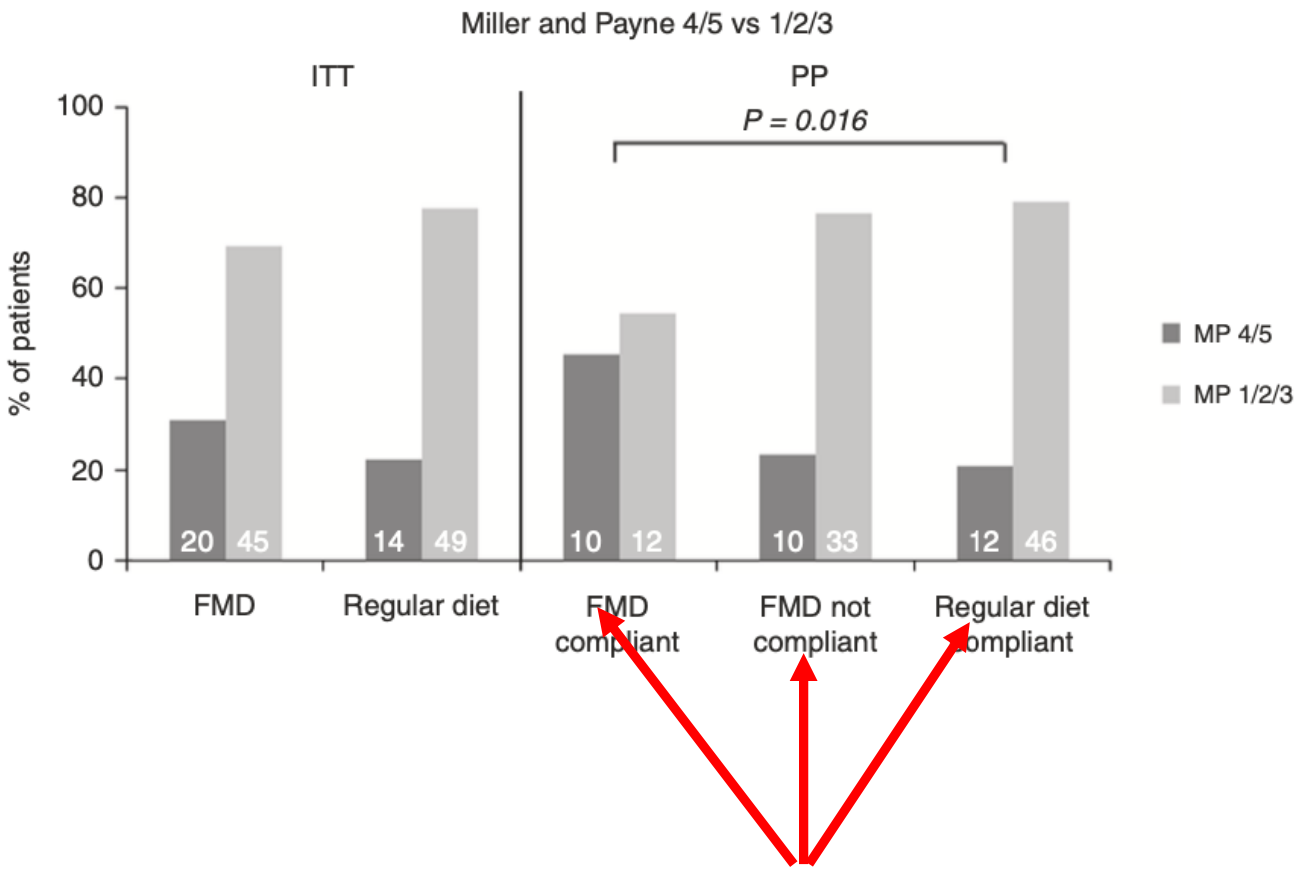
Supplementary Table 1: Miller-Payne criteria for grading pathological response after neoadjuvant chemotherapy.

MP Grade	*PATHOLOGICAL CHARACTERISTICS OF THE PRIMARY TUMOR*
1	*No change or some alteration to individual malignant cells but no reduction in overall Cellularity*
2	*A minor loss of tumor cells but overall cellularity still high; up to 30% loss.*
3	*Between an estimated 30% and 90% reduction in tumor cells.*
4	*A marked disappearance of tumor cells such that only small clusters or widely dispersed individual cells remain; more than 90% loss of tumor cells*
5	*No malignant cells identifiable in sections from the site of the tumor; only vascular fibroelastotic stroma remains often containing macrophages. However, ductal carcinoma in situ may be present.*

Studie 2 Tumoransprechen



Studie 2 Tumoransprechen



Studie 2

Table 1 Patient characteristics.

	FMD ($N = 65$)	Regular diet ($N = 64$)
Median age (range), Years	49.0 (31–71)	51.0 (27–71)
Median body mass index (range), kg/m^2	25.7 (19.8–41.2)	26.0 (19.7–39.0)
WHO status		
Grade 0	61 (93.8%)	60 (93.8%)
Grade 1	3 (4.6%)	4 (6.3%)
Unknown	1 (1.5%)	0 (0%)
Menopausal status		
Pre/Peri	27 (41.5%)	31 (48.4%)
Post	38 (58.5%)	31 (48.4%)
Unknown	0 (0%)	2 (3.1%)
T-classification		
T1	5 (7.7%)	6 (9.4%)
T2	42 (64.6%)	41 (64.1%)
T3	17 (26.2%)	15 (23.4%)
T4	1 (1.5%)	2 (3.1%)
N-classification		
N0	29 (44.6%)	33 (51.6%)
N1	28 (43.1%)	26 (40.6%)
N2	7 (10.8%)	4 (6.3%)
N3	1 (1.5%)	1 (1.6%)
Stage		
I (ineligible)	0 (0%)	1 (1.6%)
II	51 (78.5%)	48 (75.0%)
III	14 (21.5%)	15 (23.4%)
HR status		
ER−/PR−	14 (21.5%)	7 (10.9%)
ER-/PR unknown	0 (0%)	1 (1.6%)
ER+/PR−	9 (13.8%)	9 (14.1%)
ER+/PR+	42 (64.6%)	47 (73.4%)
Chemotherapy regimen		
AC-T	52 (80.0%)	47 (73.4%)
FEC-T	13 (20.0%)	17 (26.6%)
Grade (BR)		
I	2 (3.1%)	2 (3.1%)
II	43 (66.2%)	42 (65.6%)
III	20 (30.8%)	19 (29.7%)
Unknown	0 (0%)	1 (1.6%)
Tumor type		
Ductal	53 (81.5%)	49 (76.6%)
Lobular	9 (13.8%)	13 (20.3%)
Other	3 (4.6%)	2 (3.1%)

FMD Fasting mimicking diet, *HR* hormone receptor, *AC-T* doxorubicin/cyclophosphamide followed by docetaxel, *FEC-T* Fluorouracil/epirubicin/cyclophosphamide followed by docetaxel, *BR* Bloom Richardson, *ER* estrogen receptor, *PR* progesterone receptor.

Studie 2: Interpretation

- Grösste Studie, welche den Effekt des Fastens beim Menschen untersuchte
- Primär Endpunkt: Toxizität: negative Studie
- Primärer Endpunkt: Ansprechrate: positiv (Subgruppe)
- 50% der FMD-Patienten mussten vorzeitig die Diät beenden
- Gewichtsverlust unter Fasten nicht beobachtet

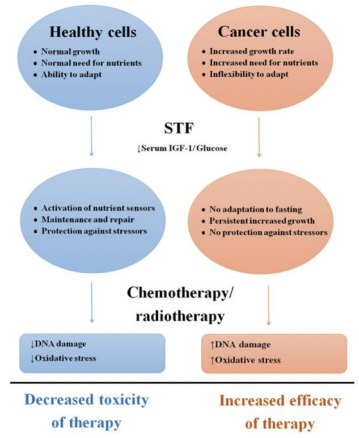


Fig. 1 Schematic overview of differential effects of short-term fasting on healthy and cancer cells. Abbreviations: STF; short term fasting, IGF-1: insulin growth factor-1.

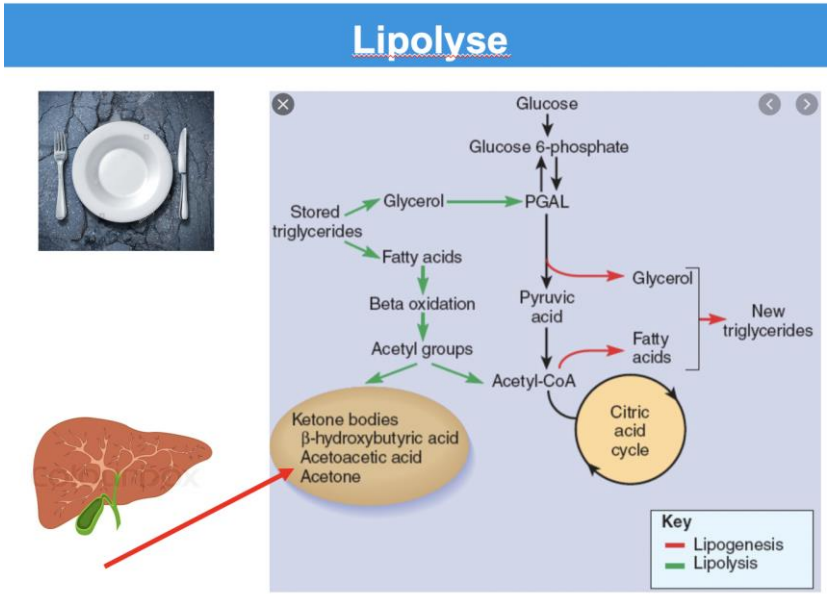
Schlussfolgerung STF bei Krebspatienten

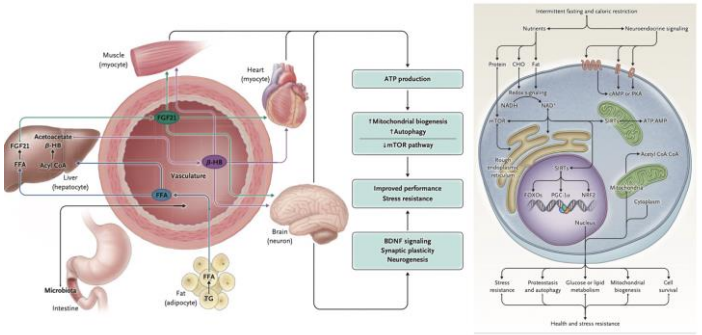
- Marginale Studienlage; zu früh für differenzierte Schlussfolgerungen
- Erste Resultate (Effektivität, NW) nicht überzeugend
- Grössere Studien dringend notwendig
- Kein relevanter Gewichtsverlust unter STF beobachtet

Ketogene Diät

Ketogene Diät

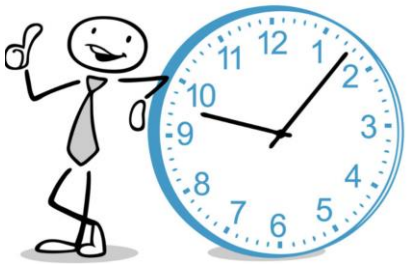
Benefit des Fastens

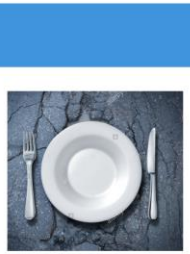


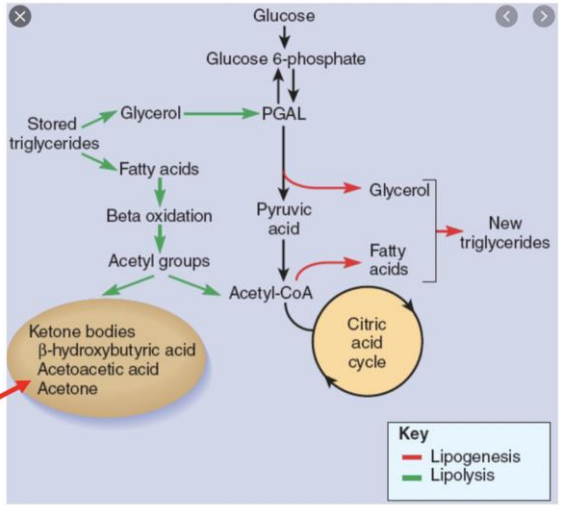


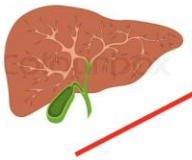
FGF21 = Fibroblast growth factor 21
β-HB = Beta-Hydroxybutyrat
} Transkriptionsfaktoren

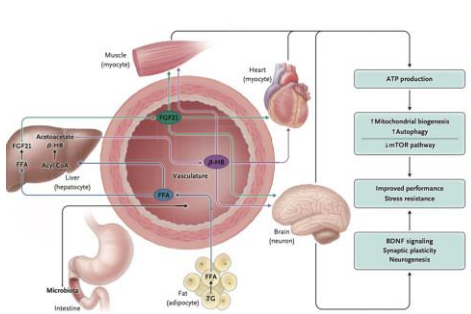
Ketogene Diät

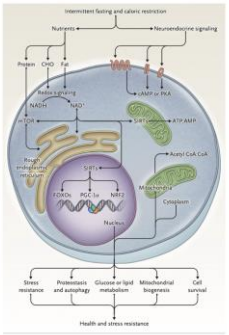






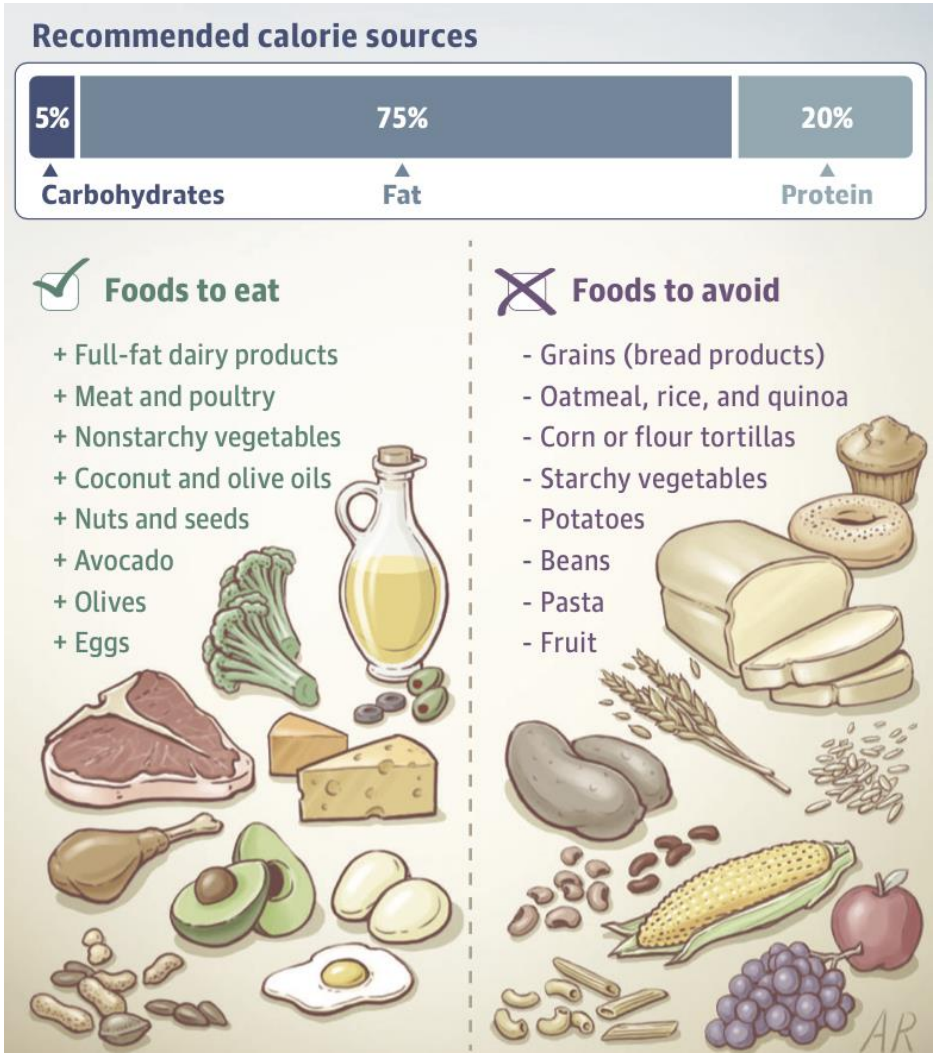


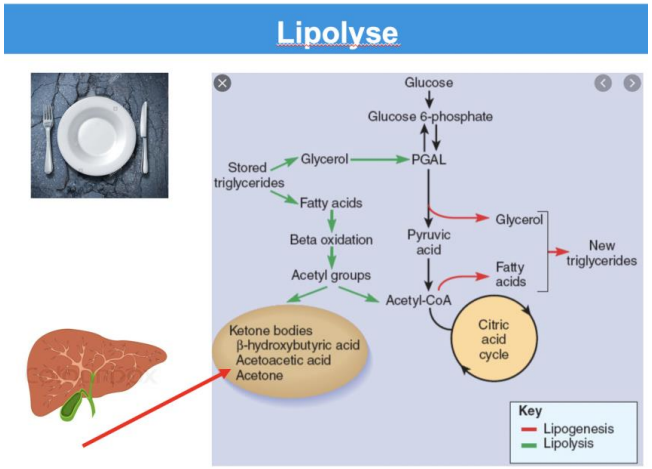


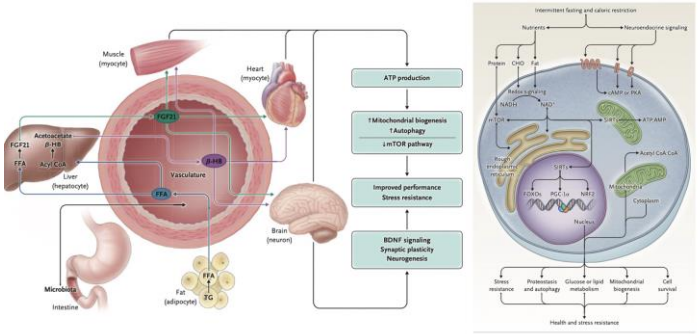


FGF21 = Fibroblast growth factor 21
β-HB = Beta-Hydroxybutyrat
} Transkriptionsfaktoren

Ketogene Diät







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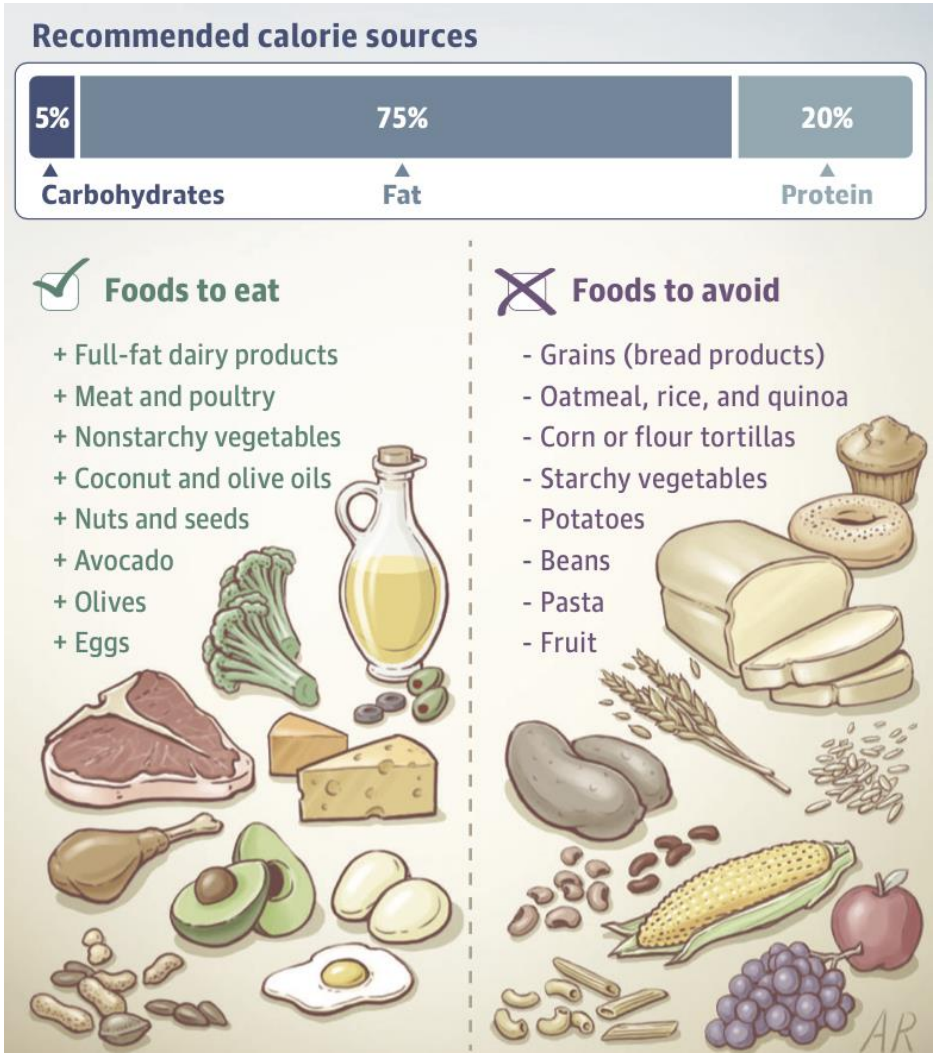

Keine international anerkannte Definition !!!

Onkologische Studien bzg KD

Table 1 Overview of studies on the ketogenic diet (KD) in cancer patients and their designs

Study	Year	Tumor	Type	Controlled	Randomized	N_{KD_ini}	N_{Ctr_ini}	N_{KD_fin}	N_{Ctr_fin}	OS
Rieger [33]	2014	Glioma	Pro	Yes	No	7	28	7	28	No
Zahra [35]	2017	Pancreas	Pro	No	No	2	0	1	0	Yes
		Lung	Pro	No	No	7	0	2	0	Yes
Cohen [36]	2018	Ovarian; Endometrial	Pro	Yes	Yes	37	36	25	20	No
Furukawa [43, 44]	2018	Rectal	Retro	Yes	No	10	14	7	13	No
Martin-McGill [13]	2018	Glioma	Pro	No	No	6	0	4	0	No
Ok [37]	2018	Pancreas	Pro	Yes	No	20	10	10	9	No
Iyikesici [40]	2019	Lung	Retro	No	No	44	0	42	0	Yes
Iyikesici [41]	2019	Pancreas	Retro	No	No	25	0	25	0	Yes

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REVIEW ARTICLE

Ketogenic diets in medical oncology: a systematic review with focus on clinical outcomes

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Schlussfolgerung ketogene Diät

- Sehr verlockendes Konzept für die Onkologie (metabolischer Zustand des Fastens mit Kalorienzufuhr)
- Weitere Forschung dringend notwendig
- Kann in dieser Form im jetzigen Zeitpunkt nicht empfohlen werden

Zusammenfassung

- Biologische Rationale für Fasten / ketogene Diät auf Zellebene sehr überzeugend

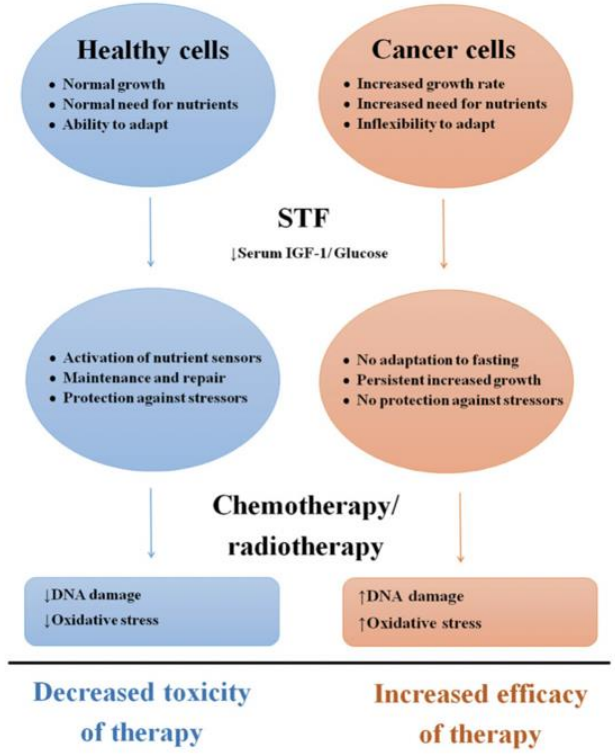

Fig. 1 Schematic overview of differential effects of short-term fasting on healthy and cancer cells. Abbreviations: STF; short term fasting, IGF-1: insulin growth factor-1.

Differential Stress Resistance

Mensch ≠ 1 Zelle

Zusammenfassung

- Biologische Rationale für Fasten / ketogene Diät auf Zellebene sehr überzeugend
- Tierversuche bestätigen mehrheitlich die theoretischen Überlegungen
- Beim Menschen: Keine gesicherte Daten bzgl. Verbesserung der Therapieverträglichkeit, Lebensqualität oder Tumoreffekt
- Erste Resultate beim Menschen zeigen, dass bei gewissen Patienten Fasten unter Begleitung (Ernährungsberatung, Arzt) vertretbar ist (Cave nicht katabole Patientin!!!!!)
- Mehr Forschung (Dauer STF) / mehr Studien indiziert
- Primäre Prävention (Verhinderung von Adipositas!) whs am effektivsten!

Danke für die Aufmerksamkeit!