„The role of NADH in Cancer Therapy“

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What is NADH ?

What role does NADH play in Cancer Prevention and Therapy ?

NADH

- **N icotinamide- (= Vitamin B3)**
- **A denine -**
- **D inucleotide -**
- **H ydride**

- also known as reduced
- **C o e n z y m e - 1**

NADH

Is the coenzyme form of

Nicotinamide

(= Vitamin B3)

NADH

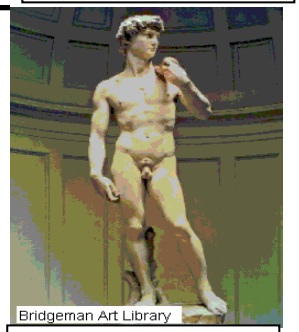
occurs in <u>all</u> organs of our body in remarkable concentrations

Heart

90 [mg / kg tissue]

Brain

40 [mg / kg tissue]



Muscles

50 [mg / kg tissue]

Blood

5 [mg / kg tissue]

Energy production in the cell by NADH

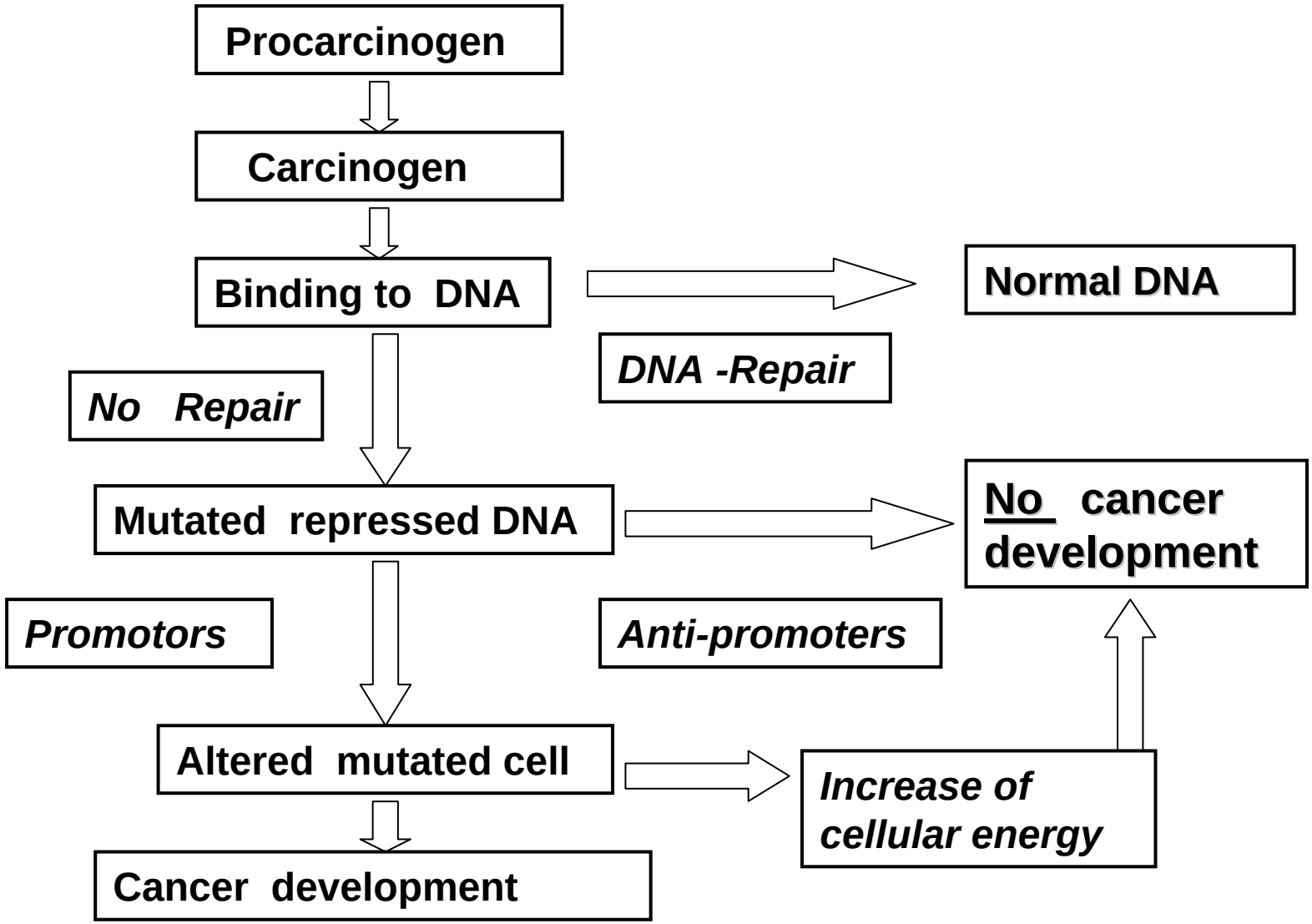
Our daily food consists of proteins, carbohydrates and lipids.

They are taken up by the organism and metabolized to amino acids, glucose and fatty acids

From these substances NADH is produced via pyruvate, and acetyl-coenzyme-A which enter the tricarboxic acid („Krebs“)-cycle where the biosynthesis takes place.

NADH reacts with oxygen present in every cell and produces ATP and water. .

The key event in carcinogenesis



The key points for cancer prevention

DNA - Repair

Anti - Promotors

Energy - Supply

The most important biological functions of **NADH**

- Essential for cell - and DNA - repair
- Powerful Antioxidant
- Fuel for cellular energy production

DNA - Repair

the 1st Step
to prevent

Cancer development

D N A - Repair

b y

NADH

The aim of the study:

- Can NADH repair cell- and **DNA – damage** ?
- What is the molecular mechanism of **DNA damage** repair by NADH ?

Doxorubicin

is a DNA – damaging substance used for chemotherapy of cancer

Cell markers used for the study

Proliferation genes (**c-myc** and **c-erbB-2**)

Apoptosis inhibition genes (**bcl-2** and **P53**)

Cell apoptosis gene (**c-fos**)

Proliferating cell nuclear antigen (**PCNA)**

Doxorubicin induces Apoptosis by blocking oncogene expression and activation of c-fos

NADH can rescue cell activity of PC12 cells from DNA damage by doxorubicin

NADH can regulate the expression of c-myc oncogen protein on PC12 cells with DNA damage

NADH repairs DNA-damage of PC12 cells by regulating of **p53** and **Bcl-2** gene protein expression

Conclusions:

- NADH promotes cell damage repair
- NADH protects cells from damage by doxorubicin
- NADH does not induce abnormal cell proliferation

- **J. Tumor Marker Onc. 13,(4) 5-17 (1998)**

NADH can repair DNA

Hence **NADH** is a cancer preventing substance

and

the more **NADH** you have in your cells the better you are off

The Reduced Coenzyme Nicotinamide Adenine Dinucleotide (NADH) repairs DNA damage of PC12 cells induced by doxorubicin

JR Zhang, K.Vreko,K.Nadlinger. D.Storga
GD.Birkmayer and G.Reibnegger

J.Tumor Marker Onco.13, 5-17 (1998)

The Reduced Coenzyme Nicotinamide Adenine Dinucleotide (NADH) rescues PC 12 cells from apoptosis

JR Zhang, K.Vrecko, K.Nadlinger. D. Storga, GD.Birkmayer, G.Reibnegger

J.Tumor Marker Oncol 13(3) 11-24 (1998)

The Reduced Coenzyme Nicotinamide Adenine Dinucleotide (NADH) Prevents Hepatic Cells from Apoptosis by Mitochondria dependant signalling Pathway

Meng XU, Jiren Zhang

Int. Journal of Modern Cancer Therapy, 3, 38-41 (2000)

Anti - Promotors

a n d

NADH

Promotors for the development of cancer

- Free Radicals
- X-rays and cosmic rays
- Ionizing radiation
- Nuclear radiation
- UV-light
- Electromagnetic fields
- Overhead power lines

Promotors for the developemnt of cancer

- Pesticides/Herbicides
- Industrial toxines
- Smoking
- Polluted water
- Immune-suppressive drugs
- Cytostatics
- Mercury (amalgam fillings)

The best Anti – Promotors are Free Radical Scavenger

The best Free Radical Scavenger are Antioxidants

The substance with the highest
Redox potential
has the highest
antioxidative capacity

NADH

as

the anti-oxidative protection shield

The antioxidative capacity of ENADA-NADH in humans

Reibnegger G, Greilberger J, Juergens G. and Oettl K.

ICMAN Proceedings,

J.Tumor Marker Oncol. 18, 37-41 (2003)

Study Results

- When LDL –cholesterol is oxidized in vitro induced by peroxyl radicals **NADH** reveals an antioxidant effect identical to vitamin C during the first 90 minutes.

- However , after 90 minutes vitamin C has no further effect while **NADH** is still acting antioxidatively

- “ While there is no such thing as a singularly ‘most important’ compound in the body or even a ‘most important antioxidant’, **NADH** comes as close as a single compound can.
- **NADH** is both the primary coenzyme that drives reduction and oxidation reactions in cellular metabolism and the most important antioxidant “
- Richard A. Passwater, Ph.D.

Oral NADH effects blood pressure,lipid peroxidation and lipid profile in spontaneously hypertensive rats

Busheri N,Taylor J,Lieberman S,Mirdamadi-Zonosi N, Birkmayer G, Preuss HG.

Geriat.Nephrol.Urol. 18(2) 95-100 (1998)

Energy Supply

b y

NADH

NADH

the fuel for cellular energy production

NADH reacts with with oxygen we breath and produces energy in form of ATP (= Adenosin-Tri-Phosphate)

Metabolic and Energetic Changes During Apoptosis in Neural Cells

- **J.C.Mills, D.Nelson, M.Erecinska and R. Pittman**
  Journal of Neurochemistry (1995)

- These cells , upon exposure to stimuli that cause single-stranded DNA breaks, experience a large increase in poly (ADP-ribose) polymerase activity, which leads to depletion of cellular **NADH**

- **The loss of NADH is thought to lead to ATP depletion, which, in turn, leads to <u>cells death</u>.**

Can we increase the energy production of a cell ?

<u>Yes,</u>

by

N.A.D.H.

N A D H-supplementation decreases pinacidil-primed $I_{K(ATP)}$ in ventricular cardiomyocytes by increasing intracellular ATP

Pelzmann B, Hallström S, Schaffer P, Lang P,Nadlinger K, Birkmayer GD, Vrecko C, Reibnegger G and Koidl B

. **Brit. J. Pharm. 2003 139, 749-754**

In neoplastic cells
energy production
via
oxidative phosphorylation
is reduced as compared to
normal cells

Hence neoplastic cells
have not enough energy to produce

all the proteins, glycoproteins
and glycolipids on the cell
membrane

essential for
regulating the cell cycle
and proliferation

If this assumption is correct

the growth of neoplastic cells

should be inhibited by

NADH

Effect of Extracellular NADH on Human Tumor Cell Proliferation

Slade N, Storga-Tomic D, Birkmayer GD, Pavelic K, Pavelic J.

ANTICANCER RESEARCH
19 : 5355-5360 (1999)

Study Results:

- NADH was very potent in inhibiting the growth of murine fibrosarcoma and human Hep-2 cells (laryngealcarcinoma)

- One dose of NADH for 4 days was sufficient in reducing the growth rate up to 92%

Treatment of cancer patients

with **NADH**

Prostate Cancer

- Patient, 59 y, first visit Sept 98
- Prostate cancer verified by biopsy
- PSA 22.0 (Sept 98)
- Treatment protocol: ENADA-NADH 5mg
  4 tablets per day, no surgery no radio-
  no chemotherapy
- PSA 8.0 (Jan. 99)
- Oct.99 control biopsy: all 8 specimen negativ,
  MRT negativ, PSA 2.5
- Mai 2003 patient in excellent health working as
  manager of an international airline

Prostate Cancer

- Patient, 63y, first visit Nov. 2002
- Prostate cancer veryfied by biopsy (6 out of 7 positiv
- PSA 16,8
- Treatment protocol: ENADA-NADH 5mg
  4 tablets per day, no surgery, no radio- no chemotherapy,
- Patient was taking already Selenium, Vit E and Vit C
- Jan. 2003: PSA 5,2
- Apr. 2003: PSA 1,6 , control biopsy: negativ,
  MRT negativ

Mamary Carcinoma

- Patient, 55y, first diagnosis Feb 1992: „ lymph node metastasis of a poorly differentiated mammary carcinoma with lymph node metastases in the neck
- Primary tumor could not be detected
- CA 15.3 : 37.0, CEA: 13.5; TPS 145
- Patient denied chemo- and/or radiotherapy
- Treatment protocoll: ENADA-NADH 5mg : 4 tablets per day,
- March 1993 : lymph node metastasis had disappeared
- CA 15.3: 15.0, CEA 8.0, TPS 95
- June 1994: CT-Scan and bone scintigraphy negative
- Jan. 2003: patient in good health with no evidence of cancer

Lung Cancer

- Patient: Male 48 y , small cell bronchial carcinoma
- Diagnosed by MRT and veryfied by biopsy Jan 2001
- Tumor size 6 to 8 cm
- Received radio- and chemotherapy for 5 month
- No change in tumor size
- Visit in Vienna in Sept 2001
- Treatment protocoll: ENADA-NADH 5mg 4 tabs/day
- In addition: Selenium, Vit E , Vit C and shark cartiladge
- Jan. 2002: Tumor mass reduced to 1,5 to 2 cm
- July 2002 : MRT negativ, no tumor mass could be detected (see following email)

Colon Cancer

- Patient: Male 65 y , colon carcinoma of the rectum
- Diagnosed by MRT and veryfied by biopsy Aug 2005
- Tumor size 8 cm
- Patient refused surgery, radio- and chemotherapy
- Started NADH treatment in Sept 2005
- Treatment protocoll: NADH 10mg (sublingually)
- 4 tabs NADH /day (in total 40 mg NADH)
- In addition: L-Arginin 1500 mg / day
- July 2007: Tumor mass reduced to 1,5 to 2 cm
- No detectable metastases.

Osteosarcoma

- Patient: Boy 13 y , ostesarcoma (pea size tumor under the tongue)
- Tumor (1cmin size) was surgically removed October 2003
- Histopathology revealed osteosarcoma
- Parents of the boy refused chemotherapy
- Boy started taking NADH March 2004
- Treatment protocoll: NADH 10mg (sublingually)
- 3 tablets NADH /day (in total 30 mg NADH)
- No recurrences of osteosarcoma or metastases since then.

Cancer with liver metastases

- Patient: Male 63 y , renal cell carcinoma,
- Diagnosed by CT February 1998
- Nephrectomy March 1998

- Detection of 3 liver metastases in April 2006
- Size of the 3 liver metastases 5 – 6 cm in diameter
- 2 cycles of chemotherapy yielded no tumor mass reduction
- Started NADH treatment in Aug 2006
- Treatment protocoll: NADH 30mg oral (in the morning)
- 3 sublingual tablets NADH (in the afternoon)
- (in total 60 mg NADH per day)
- Additional supplements : L-Arginin 1500 mg / day
- Aug 2007: Mass of all 3 metastases reduced to 1,5 to 2 cm
- Patient physically and mentally in very good condition.
- Back again as boss of his own company since Jan. 2007

Types of Cancers treated with NADH

- Prostate Cancer: 19 cases; 10 *TR* , 9 *TF*
- Mammary Carcinoma: 3 cases; 1*TR* , 2 *TF*
- Colon Cancer : 3 cases; 3 *TR*
- Small Cell Lung Cancer: 3 cases; 2 *TR* 1 *TF*
- Non-Hodgkin Lymphoma: 3 cases; 2*TR*, 1*TF*
- *Osteosarcoma: 1 case; 1 TF*
- Glioblastoma: 2 cases; 1 *TR*, 1 *TF*
- *TR = Tumor Regression*
- *TF = Tumor Free*