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Evaluation of the nutritional status of a cancer patient

The basic science of weight loss: What should oncologists know?

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Cancer and nutrition

↑ Mortality

↑ Morbidity

↓ Quality of life

↑ Sanitary costs

Undernutrition

Cachexia

Cancer
marked weight loss, anorexia, asthenia and anemia
Mild weight loss anorexia

Moderate weight loss anorexia

Severe weight loss anorexia

Metabolic changes

Reduced activity

Muscle wasting obvious

Reduced survival

Death

Normal
**CACHEXIA**

**% of patients with weight loss**

- Gastric
- Pancreas
- Lung
- Prostate
- Colon
- Breast

**Survival (weeks)**

A problem of energy balance

Anorexia

Reduced food intake

Metabolic alterations

Increased energy expenditure
TOTAL ENERGY EXPENDITURE (TEE)

BASAL METABOLIC RATE (REE)
DIET-INDUCED THERMOGENESIS (DIT)
PHYSICAL ACTIVITY (PA)

TEE = REE + DIT + PA
TOTAL ENERGY EXPENDITURE (TEE)

Healthy

Cancer
ENERGETIC INEFFICIENCY

FUTILE CYCLE ACTIVITY

TUMOUR

GLUCOSE → LACTATE

GLUCOSE ← LACTATE

INCREASED THERMOGENIC ACTIVITY

UCP1 ACTIVITY IN BAT

OTHER UCPs (?)

LIVER

H⁺ → ATP + Pi

MITOCHONDRIA

UCP1

RESPIRATORY CHAIN

H⁺
Cori cycle (Tumour-Liver)

Liver

Glucose

Lactate

- 6 ATP

Tumour

Glucose

Lactate

+ 2 ATP

Energetic balance = - 2 ATP
The UCP Family

- **UCP1**: Brown adipose tissue (BAT)
- **UCP2**: Ubiquitous
- **UCP3**: Skeletal muscle and BAT
- **UCP4**: Neural tissues
- **UCP5**: Neural tissues (BMCP-1)
Multiorgan syndrome
Systemic disorder
The Cachexia Pyramid

- **Weight loss**
- **Skeletal muscle**
- **Tumour**
- **Treatment**
- **Food intake**
- **Metabolic abnormalities**
- **Tumour factors**
- **Cytokines**
- **Hormones**
- **Brain**
- **Immune system**
- **Liver**
- **Skeletal muscle**
- **Adipose tissue**
- **Blood**
- **Gut**
- **Immobility**
- **Quality of life**
- **Weight loss**
- **Anemia**
- **Oedema**
- **Weakness**
Mechanisms
Anorexia
Molecules involved in cancer anorexia ??

Cytokines
Circulating hormones
Neuropeptides
Neurotransmitters
Amino acids
Tumour-derived factors
Anorexigenic Neuropeptide

- Neurotensin
- CART
- GLP-1
- Melanocortin
- CRF

Orexigenic Neuropeptide

- MCH
- Orexin
- Galanin
- Opioid
- NPY

Blood-brain barrier

Blood intake

Food intake

E expenditure

Blood

Vague nerve

Glucagon

Leptin

CCK
**CART**

**Neurotensin**

**CART**

**GLP-1**

**Melanocortin**

**Neuropeptide**

**Orexigenic Neuropeptide**

**Orexin**

**Galanin**

**Opioid**

**NPY**

**Blood-brain barrier**

**Food intake**

**E expenditure**

**CNS**

**Cytokines**

**IL-1**

**IL-6**

**TNF-α**

**IFN-γ**

**IFN-γ**

**glucocorticoids**

**ACTH**

**Blood**

**Vague nerve**

**Blood-brain barrier**

**Leptin**

**Glucagon**

**CCK**

**CNTF**

**IL-1**

**IL-6**

**NPY**

**CRM**

**Serotonin**

**Trp**

**MCH**

**Leptin**

**Glucagon**

**CCK**
Metabolic alterations

Skeletal muscle
CANCER CACHEXIA

PROTEIN

K\textsubscript{d}  \quad \uparrow  \quad K\textsubscript{s}

AMINO ACIDS
Peptides

26S Proteosome

Protein

E1 Ubiquitin

E2

Proteolysis

Activation

ATP

Conjugation

Proteosome 26S

Peptides
Ubiquitin mRNA levels in skeletal muscle of gastric cancer patients

Patients lost 5.57% of body weight (n= 20)

Apoptosis
Apoptosis in gastro-intestinal cancer patients

Figure 1 Skeletal muscle apoptosis in cancer patients. For further details, see the Materials and methods section. DNA fragmentation was assessed by monitoring the laddering in an agarose gel. The results are expressed as % of DNA fragmentation. The results are mean values ± S.E.M. of a minimum of five samples. C+: 40 μg of liver DNA from anti-Fas-treated mice (positive control). C: control group, CAN: cancer patients. Values that are significantly different by the Student’s t-test from the non tumour-bearing patients are indicated by *p < 0.01.
Fig. 1. Caspase-3: apoptosis and protein degradation signalling.
Mediators
IL-4
IL-10
IL-15
IL-1ra
sIL-6R
sTNFR

ANTI-CACHECTIC FACTORS

IL-1
TNF
IL-6

PRO-CACHECTIC FACTORS
Signaling
SIGNALS

TRANSDUCTION PATHWAYS

EFFECTS

MUSCLES

LIVER
Signaling

Argilés et al., 2008  Int. J. Biochem. 40, 1674

Fig. 2. The role of PI3K in signalling protein turnover in skeletal muscle.
CACHEXIA

TNF & other cytokines

UCP 3

NF-κB, AP-1

ROS

DNA fragmentation 
APOPTOSIS

UB-DEPENDENT 
PROTEOLYSIS

Energetic 
inefficiency

PROTEASOME
Intervention?
Developing cancer-specific nutritional approaches

Objectives

- Increase body weight
- Stimulate food intake
- Decrease inflammation
- Decrease energy expenditure
- Enhance absorption/Gastric emptying
- Preserve LBM (anabolic + anticatabolic)
- Enhance QoL
- Control cancer
- Promote health
Thank you!