Optimal preparation for cancer treatment
Dr Jann Arends • Tumor Biology Center • Freiburg • Germany

Improving disease management and clinical outcomes through Advanced Medical Nutrition
Introduction

Nutritional problems follow the cancer patient.. everywhere..

2 major elements:
- Metabolism
- Immunology
Development of cancer

Immunesurveillance

A. Initiation

B. Promotion

C. Malignant Conversion

Inflammatory progression

D. Progression

E. Metastasis
Immune activity and cancer

Johansson et al., 2008
DeNardo & Coussens, 2007

**Immune surveillance - inflammatory progression**

### Acute Inflammation
- **Th1**
  - IL-2
  - INFγ
- **B cell**
  - Anti-tumor Ig
- **Tumor Rejection**
  - M1 Macrophage polarity
  - Innate anti-Tumor Cell Cytotoxicity
  - CTL Mediated Killing

### Chronic Inflammation
- **Treg**
  - IL-10
  - TGFβ
- **Th2**
  - IL-4
  - IL-10
  - IL-13
  - Stromal Ig/IC
- **B cell**
- **Tumor Promotion**
  - M2 Macrophage polarity
  - Antigen presentation
  - CTL Mediated Killing
Patient journey

- Fatigue
- Loss of appetite
- Weight loss
- Complications
- Reduced QoL
- Catabolism
- Immune defects
Patient – Clinical problems

- Catabolism
- Chronic inflammation
- Immune defects
Development of human breast carcinoma is characterized by abundant infiltration of immune cells. Representative sections of normal, premalignant, and malignant human breast tissue stained with hematoxylin and eosin (H&E) (upper panels), and following immunodetection of CD45 (leukocyte common antigen, brown staining). DCIS, ductal carcinoma *in situ*.

*DeNardo & Coussens, 2007*
Chronic inflammation in cancer

- CRP increased at diagnosis in 50% (pancreatic cancer)
- CRP correlated with
  - increased energy expenditure (Falconer 1994)
  - decreased caloric intake (Wigmore 1997)
  - decreased survival (Deans 2004)
Immune defects

- Susceptibility to infections
- Post-operative complications
- Death by infection
Prognostic factors in cancer

- Psychological stress
- Nutritional state
- Immune competence
- Systemic inflammation
- TUMOUR
- QoL

Inhibiting factors:
- Nutritional state
- Immune competence
- TUMOUR

Improving factors:
- Psychological stress
- Nutritional state
- Immune competence
- TUMOUR
Goals for oncology-specific nutrition

- Reduce inflammation
- Improve muscle function (strength and endurance)
- Improve immunity
New nutritional supplement

- Reduce inflammation
  - Eicosapentaenoic acid - EPA
- Improve muscle function
  - High protein/Leucine content
- Improve immunity
  - Oligosaccharides - FOS/GOS
Plasma fatty acids with supplement

All FAs increase/decrease significantly at all time points.

*Significantly different from baseline p < 0.001.
Data presented as mean ± standard deviation.
Plasma fatty acids with supplement

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Tumour-induced cachexia: *In vivo* model

Syngenic CD2F1 mice

Day 0: s.c.-inoculation of $5 \times 10^5$ colon adenocarcinoma cells

A and B: test for contact hypersensitivity to oxazolone (Th1-response)

**Faber et al. Br J Cancer 2008**
Significant reduction in Th1-immune function prior to weight loss

Effect of tumour inoculation on in vivo Contact Hypersensitivity measured by ear swelling in a pre-cachectic state on day 14 (A) and in mice already suffering from cachexia on day 22 (B).

*** p<0.001 between groups.

Van Helvoort et al., 2007
New supplement: Effects on inflammatory mediators

**TNF-α in plasma**

- * p< 0.001 vs Control,
- ^ 0.001<p<0.01 vs Control,
- # 0.01<p<0.05 vs Control and TB-con

Faber et al. Br J Cancer 2008
New supplement: Effects on Th1-immune function

Oxazolone contact hypersensitivity

Δ Ear thickness (µm)

Control  TB-con  TB-SUPPL

* p< 0.017 vs Control, # p< 0.017 vs TB-con

Faber et al. Br J Cancer 2008
New supplement: Effects on opportunistic infections post Ctx

**Pseudomonas infection model**

**Faecal colonization**
- Log$_{10}$[cfu/g feces] vs. time (days)
- Control vs. SUPPL
- Pathogens
- Nutritional intervention
- Infections
- Sepsis

**Liver translocation**
- Log$_{10}$[cfu/liver] vs. condition
- CTRL vs. SUPPL
- Translocation incidence: 95% vs. 60%
- *p=0.02
New supplement: Improvement muscle function

Maximal muscle force

Daily activity (day 19)

Van Norren et al. Br J Cancer 2009
**Dual mode of action**

**Anticatabolic and immune-preserving**

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<th>Actives</th>
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<td>Decreased inflammatory status</td>
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**Mechanism of action**

- **Anabolism**
  - Leucine High Protein
  - Fish oil

- **Catabolism**
  - Fish oil
“Dawn of a new era of cancer therapies”
Tlsty & Coussens, 2006

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Conclusions

- Cancer is associated with nutritional, metabolic and immunological deterioration. This makes the patients susceptible to complications or delay of treatment.

- The New Supplement (EPA, Oligosaccharides, Protein, Leucine mixture) clearly demonstrated in pre-clinical studies:
  - improvement in immune activity
  - reduction in inflammation
  - improvement in muscle function

- The improvement of the immune function, already in an early phase, will help to reduce the risk for infectious complications. This will increase the chances of an optimal execution of cancer therapies.
Imbalance of anabolism vs catabolism

During catabolic stress

First pass extraction

Leucine concentration (µM)

Cancer

normal
Optimal preparation for cancer treatment

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