Research update from NTNU

university – industry collaboration in baromedicine
The Dealing with depths project

• Four-year research collaboration (2018-21/22)

• Led from NTNU, funded by the Norwegian Research Council and Equinor via the PRSI pool

• 100% dependent on diver participation and access to TechnipFMC dive campaigns

• Focused on physiological mechanisms involved in saturation divers' health and fitness

• Also includes studies of decompression sickness in sports- and recreational divers
NORMAL ADAPTATIONS TO SATURATION DIVING

- Mild anemia development
- Changes in the divers’ bacterial flora

DISEASE AFTER DIVING

- Decompression sickness
Fatigue is common in the first days after saturation diving.

Anemia can cause fatigue, and hemoglobin levels are low in people with anemia.

We monitored 11 divers’ hemoglobin daily through a 4-week saturation dive, and for about 2 weeks after.

The divers did the hemoglobin readings themselves. We collected and analyzed the data.
The divers were mildly anemic for one week after saturation.
Over to Roxane
What happens in the oral cavity during saturation diving?
What do we know?

• **Saturation diving:** affects all life present

• **The healthy oral cavity:** home to over 700 bacterial species
  • Oral bacteria are classified according to their **oxygen needs**

• **Oral microbiota:** microorganisms inhabiting the oral cavity
  • **Interactions** with the host: symbiotic relationships to keep the host healthy
  • **Diversity** due to the host’s lifestyle or the environment of the oral cavity
Why does it matter?

• Environmental adaptations of the oral microbiota in contact with the breathing gas during the heliox saturation dive

  • Composition?
    • Identify the types of bacteria present in the divers’ mouth
Why does it matter?

- Environmental adaptations of the oral microbiota in contact with the breathing gas during the heliox saturation dive

  - **Composition?**
    - Identify the types of bacteria present in the divers’ mouth

  - **Activity?**
    - Investigate whether changes in bacterial composition affect the divers’ health and fitness
Increase of facultative anaerobes/aerobes

Decrease of obligate anaerobes

Bacterial composition
Composition of the oral microbiota

- Reduction in the bacterial complexity
- Shift of aerobic bacteria over anaerobic bacteria
- Transient changes during the heliox dive
"Vitamin B_{12} and folate are involved in the production of red blood cells and are linked to EPO activity” (Deb, Swinton, & Dolan, 2016)
Activity of the oral microbiota

- Decrease in vitamin B\textsubscript{12} biosynthesis
- Supports the nutritional recommendations for vit.B\textsubscript{12} supplements as part of the divers’ diet
Acute Effects on the Human Peripheral Blood Transcriptome of Decompression Sickness Secondary to Scuba Diving

Kurt Magri, Ingrid Eftedal, Vanessa Petroni Magri, Lyubisa Matity, Charles Paul Azzopardi, Stephen Muscat and Nikolai Paul Pace

Mapping inflammation and immune responses in decompression sickness
Decompression sickness (DCS)

is caused by dissolved gases emerging from solution in the form of bubbles inside body tissues during decompression
Why did we perform this study?

- The pathophysiology of DCS is not completely understood
- There are limited treatment options
- 10-20% of cases result in long-term sequelae
- Better understanding of the pathophysiology may identify druggable targets
The necessary ingredients for the DCS study

- Clinical competence and treatment facilities
- Analytic platforms for molecular biology and bioinformatics
- Divers with and without DCS
The grail

Malta
Cutis marmorata in divers with DCS

• A cardinal sign when appearing in divers with suspected DCS

• Appears in type 1 DCS (non-neurological), with high likelihood for progression into neurological DCS

• Hypnotized to be caused by:
  1) local formation of bubbles in the skin or blood vessels; or
  2) arterialization of venous bubbles across a right to left shunt (RLS/patent foramen ovale)
The analysis

Blood RNA extraction

Conversion to cDNA + library prep

Sequencing

Bioinformatics: Data processing and statistics

Biological interpretation
The Decompression Sickness Transcriptome

Activation of the Adaptive Immune System
- EGR3
- NR4A2
- GZM2

Activation of Immediate Early Genes

An upregulated gene set characteristic of myeloid cells

Activation of the Innate Immune System

Neutrophil Activation and Degranulation

Enrichment of Inflammatory Transcripts

Increased Cytokine Signalling (IL-4, IL-13, IL-10, TNF signalling)

Toll-like Receptor Signalling (innate activation via NF-KB)

Reversal at T2 Possible Effect of HBO

PI3K-AKT Pathway Activation
AKT pathway regulates production of ROS/RNS
Gene Expression Changes Common to Diving and DCS

Upregulation of Genes expressed by Myeloid Cells

Upregulation of Antioxidant Genes

- Glutathione Peroxidases
- Superoxide Dismutases
Main conclusions

DCS is accompanied by a dynamic regulation of inflammatory and innate immune pathways, with a pronounced increase in activity characteristic of the myeloid lineage. “

Oxidative stress: “there is prominent activation of free radical scavenging mechanisms.

When the levee breaks: Our findings reinforce the role of acute inflammation in DCS and provide evidence for a continuum between the physiological response elicited by uneventful diving and diving complicated by DCS.
How can we apply the results?

The long-term goal: Biomarker development for rapid identification of DCS vs. differential diagnoses.

Fundamental physiology: Improved understanding of the interplay between environmental stress and pathophysiological responses.
Come talk with us in the exhibition area 😊