



# **UNDERSEA & HYPERBARIC MEDICAL SOCIETY Annual Scientific Meeting 19 June 2014**

## **Office of Naval Research UNDERSEA MEDICINE PROGRAM A National Naval Responsibility**

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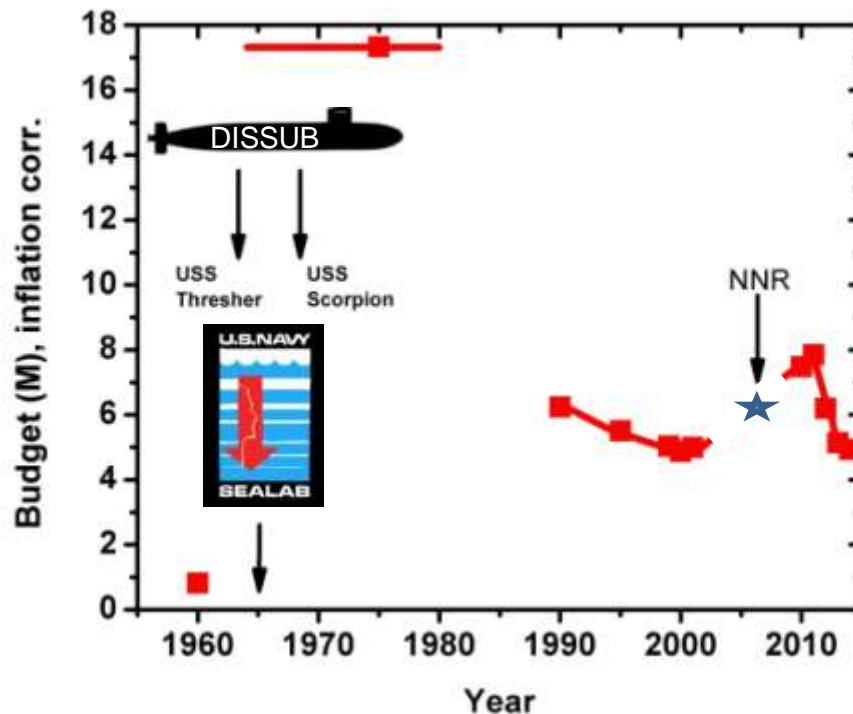
# Undersea Medicine Program Overview



- Purpose: compensate for human shortfalls in operating under water
  - Breathing, extreme pressure, cold, dark, chem/bio/rad contamination
  - Enhance human physiology, provide technology to do so (*or set limits*)
- National Naval Responsibility, ONRINST 5250.1A, 2006
  - Sustain robust international research capability and Navy labs
  - Cultivate pipeline of scientists and engineers
  - Provide S&T products that ensure future superiority in the undersea domain
- Longstanding and robust Fleet requirements
- Direct and immediate warfighter application
  - Diving and Salvage: hull repair, recovery, rescue
  - Special Warfare (SEAL & EOD): stealthy ingress, route clearance
  - Submarine Force: long missions, confined space, limited senses



# Undersea Medicine has a Rich History



## ONR funding increased dramatically in 60's

- ~\$15M in the era of the "Space Race"
- Lost sub events in 1963 and 1968
- SEALAB I and II in 1963 and 1964

## Funding level lower but constant in 90's

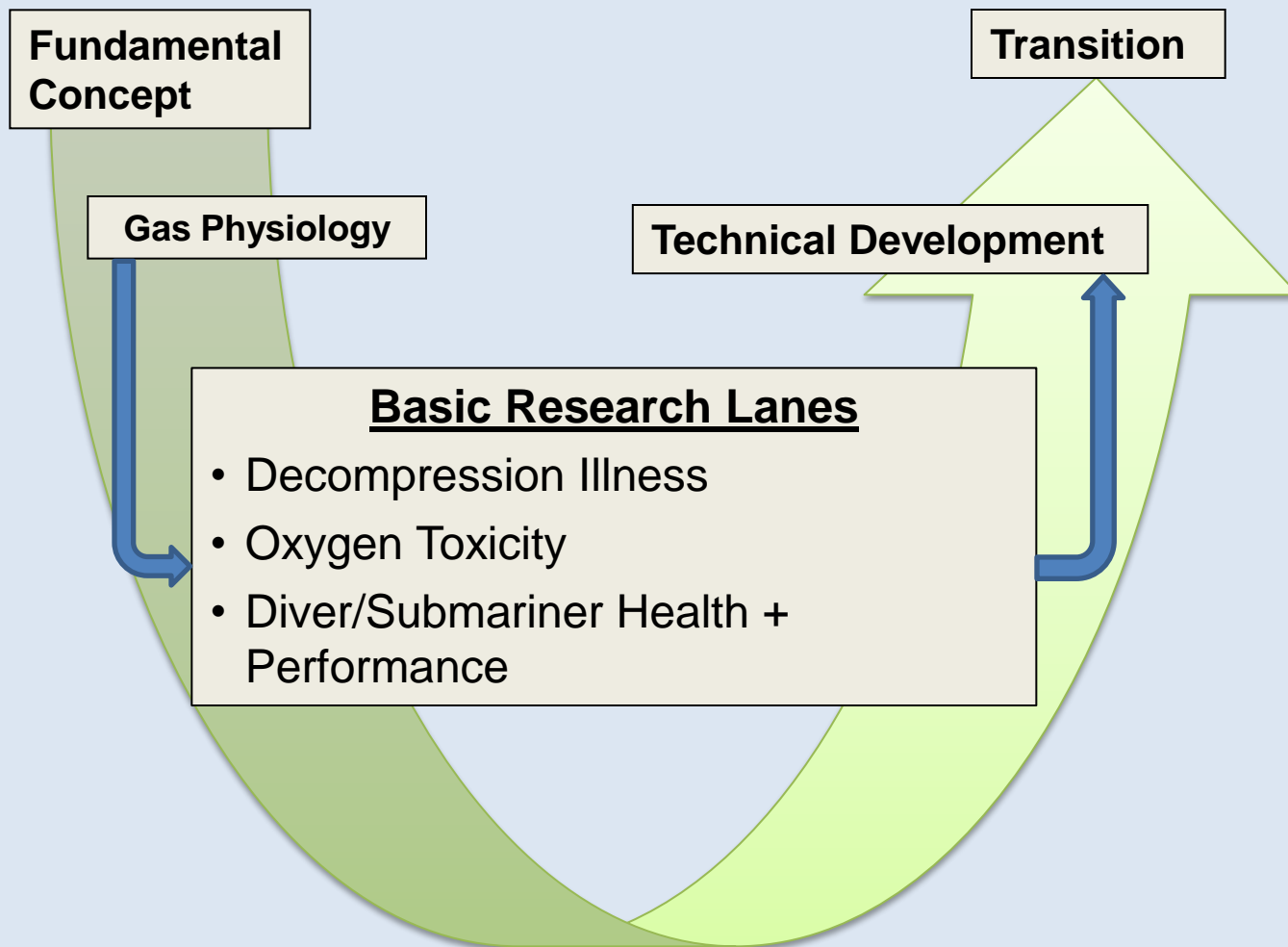
- ~\$5M

## National Naval Responsibility in 2006

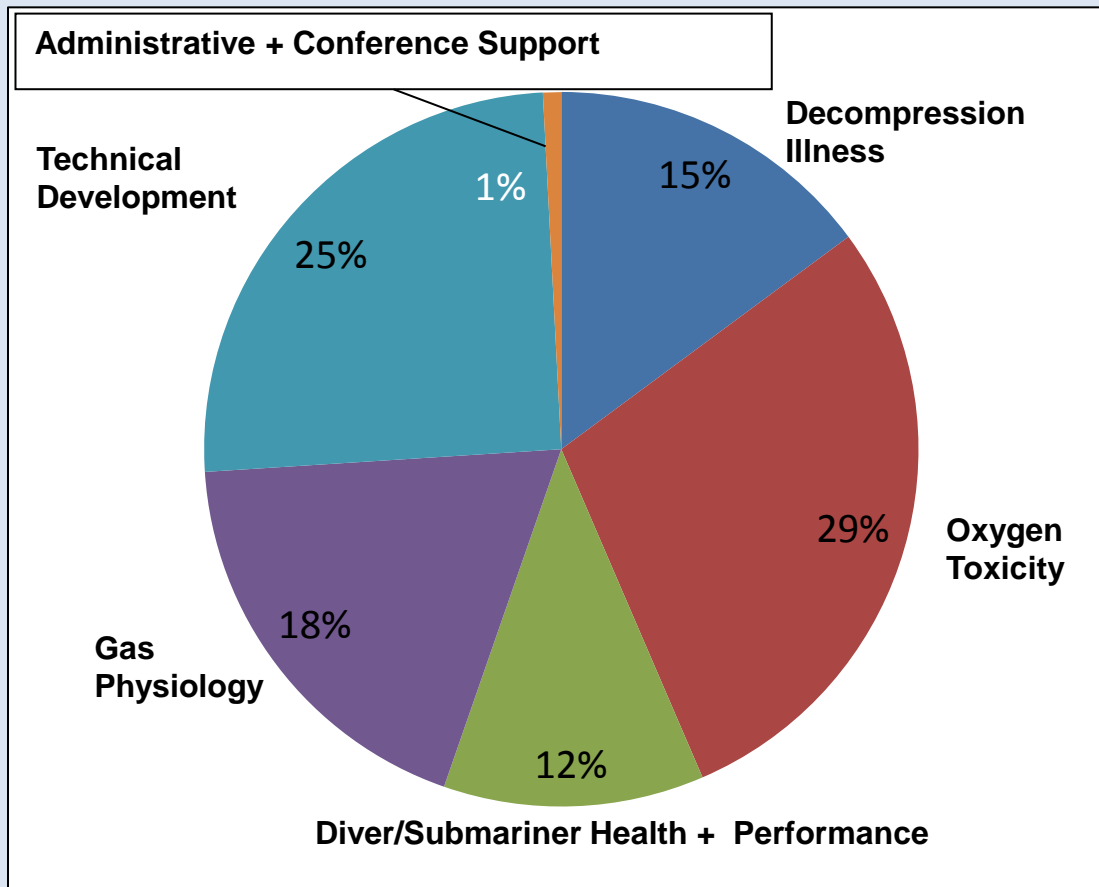
## Program boosted around 2010

- Perfluorocarbon for decompression
- Women in Submarines program

# UMed Focus and Pathway



# Current Investment Portfolio



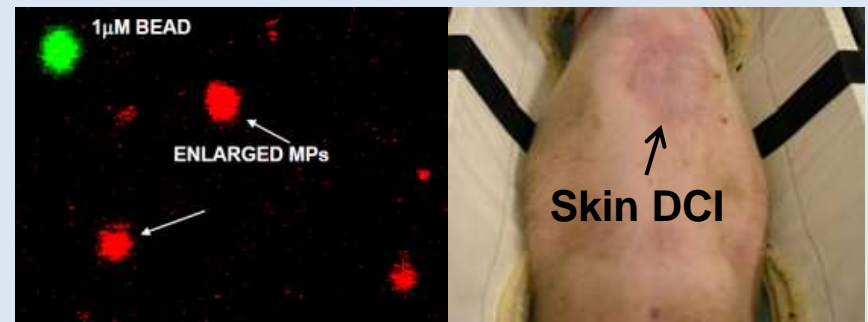
- Divers and submarine escapees at risk for decompression illness (DCI)
- Initiation: formation of bubbles in the blood and tissue with decreased pressure
- Mechanisms of bubble formation unknown
- Current mitigation strategy: diving tables
  - Conservative approach
  - Limit operational capability
  - Not 100% reliable
  - Not real-time
  - Not individualized
- DCI is treated with a hyperbaric chamber
- Therapy not involving a chamber is desired
- Understanding the etiology of DCI will support the development of better decompression tables and pharmaceutical interventions
- Goal is increased operational diving capability and improved submarine escape

## Current basic research efforts

- Microparticle Production with Decompression Stress
- Microparticles, Platelet-Neutrophil Aggregation and Decompression Sickness
- Probabilistic Decompression Modeling

## Key Performers

- Naval Medical Research Center
- Navy Experimental Diving Unit
- University of Maryland
- University of Pennsylvania
- Duke University
- Dartmouth College





# Research Lane: Oxygen Toxicity



- Naval Special Warfare divers at risk for hyperbaric oxygen (HBO) toxicity
  - While using re-breathers and delivery vehicles
  - Mitigation by depth-duration limits on operations
- HBO toxicity ( $O_2$  intoxication or poisoning) symptoms
  - Central nervous system: Disorientation, tinnitus, nausea, anxiety, seizures, unconsciousness
  - Pulmonary: Difficulty breathing, coughing, chest pain, collapsed lung
  - Ocular: Tunnel vision, myopia, retinal detachment
  - Minor symptoms can be overlooked/confused
  - Onset unpredictable: depends on exposure, individual and day-to-day differences, immersion, temperature and exercise
  - Robust recovery is typical
- The pathophysiology of oxygen not well understood
  - Biochemical basis thought to be reactive oxygen species
  - Oxidative damage occurs at the cellular level, including the cell membrane
- Understanding the etiology of HBO toxicity will lead to pharmaceutical/physiological interventions

## Current basic research efforts

- Cellular Mechanisms of CNS Oxygen Toxicity
- Fellowship for Probing the Molecular Origins of Cell Membrane Damage in Hyperbaric Oxygen Toxicity
- Efficacy and Anticonvulsant Mechanism of Ketogenesis in CNS Oxygen Toxicity
- Nitric Oxide and CNS-Pulmonary Interactions in  $O_2$  Toxicity

## Key Performers

- Naval Medical Research Center
- Navy Experimental Diving Unit
- University of South Florida Tampa
- Duke University.



Exploring biomarkers for impending seizure





# Research Lane: Submarine/Diver Health and Performance



- Operational limitations in severe environments
  - Extreme temperature
  - Lack of light
  - Damaging noise levels
  - Psychophysical differences
  - Physical and cognitive endurance
  - Chemical/biological exposures
  - Team performance
- Mastering environment essential for achieving an operational edge
  - Submariners on long missions
  - SEALs making an unexpected ingress

## Current basic research efforts

- Enhancing Human Underwater Sound Localization Abilities Via Mechanical and Electronic Manipulation of the Acoustic Signal
- Postdoctoral Research Fellowship in Underwater Psychoacoustics/Spatialized Audio

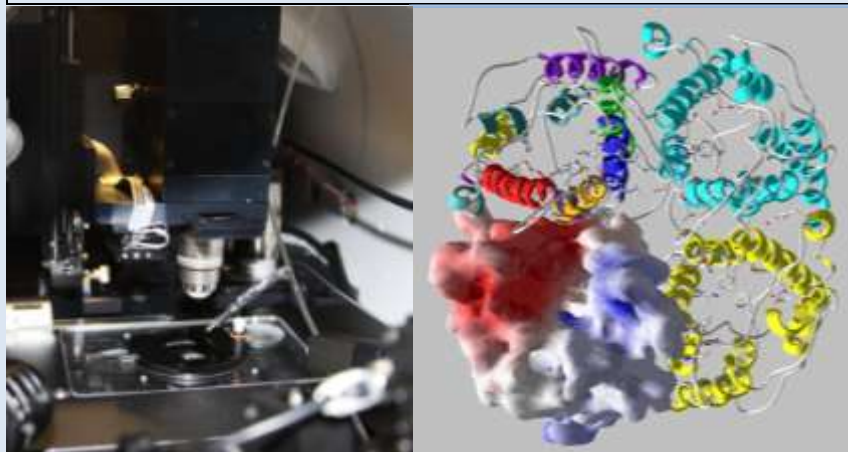
## Key Performers

- Naval Submarine Medical Research Lab





- Breathing and “Inert” gas uptake/elimination
  - Vascular and tissue gas concentration
  - Mechanisms of gas exchange
  - Gas transport through channels
  - Membrane mechanics and permeability
  - Cellular function changes with pressure
  - Noble gas effects on ionic conductance
- Compare across species
  - Humans, marine mammals, lab models
- Learn from the special cases
  - Solubility of  $N_2$  in adipose tissues
  - Absorption of  $CO_2$  by the gastric system
- Goal is pharmacological control of gas transport



## Current basic research efforts

- Gas Transport
- Postdoctoral Fellowship for Gas Transport through Protein Channels
- Effect of Gas-Pressure Combinations on Cellular Electrophysiology (patch clamp)
- Nitrogen Solubility in Adipose Tissues of Diving Animals: Implications for Human Divers and for Modeling Diving Physiology
- The Role of Gastric Ventilation in Maintaining Normocapnia
- Probing the Molecular Origins of Cell Membrane Damage in Hyperbaric Oxygen Toxicity

## Key Performers

- Navy Experimental Diving Unit
- Case Western Reserve University
- University of North Carolina Wilmington
- University of South Florida Tampa
- University of Southern California



# Focus Area: Technical Development



## Current research efforts

- Evaluation and Testing of Carbon-based Hydrophobic Electrocardiogram Electrodes
- Evaluation of the effects of CNS oxygen toxicity and hyperbaric environments on the autonomic nervous system, utilizing Principal Dynamic Mode Analysis
- Pharmacological Inhibition of Neutrophil Adhesion using Nitric Oxide
- Perfluorocarbon emulsion as adjunct treatment for DCS with subsequent HBO therapy (HBOT)
- Using Tiotropium Bromide for Reducing the Incidence of Pulmonary Oxygen Toxicity Associated with Hyperbaric Oxygen Exposure
- Optimizing Mixed Gas Rebreathers for Helium Conservation and Diver Safety to enable Rapid Response Deep Diving

## New effort

- Effects of Adenocaine® on survival following drowning in rats

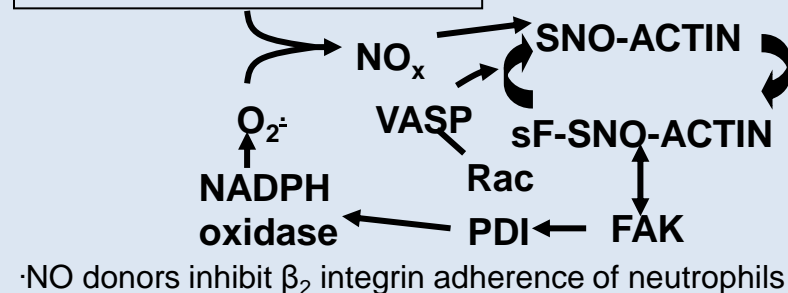
## Applied research a strong element of UM

- Testing of pharmacological treatments
- Human factors of technology for divers
- Development of advanced research methods
- Opportunities for 6.3 funding

## Key Performers

- Naval Medical Research Center
- Navy Experimental Diving Unit
- Naval Surface Warfare Center Panama City
- University of Maryland
- Worcester Polytechnic Institute

## **Nitric Oxide donor drug**





# Partnering with Industry: Strong UM SBIR/STTR Track Record



## Small business program a good fit for UM topics

- Human factors of technology for divers
- Development of research methods

### Phase I completed (Jan 2014)

- Prehensor For 1 Atmosphere Diving Suit
- Lightweight Atmospheric Diving Suit

### Phase II underway

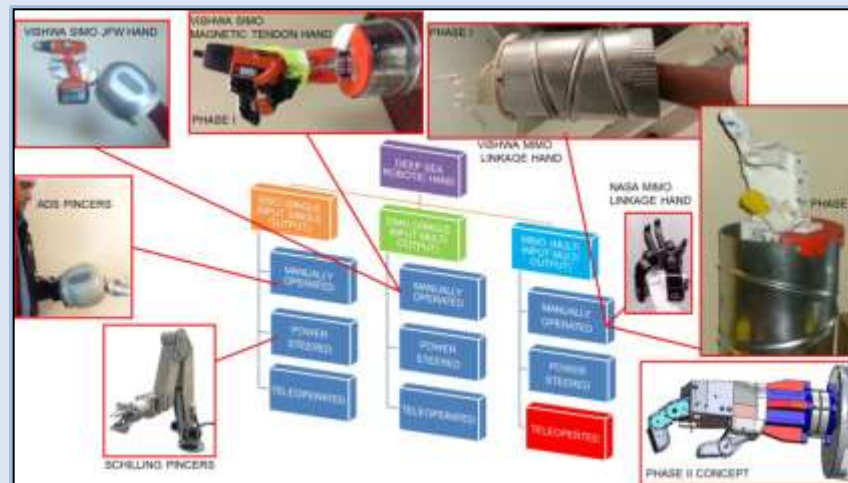
- Dive Helmet Noise Quieting
- Hand-held Submersible Real-time Reagentless CBE Sensor
- fMRI Compatible Hypo-hyperbaric System for Diving Research and Hyperbaric Medicine
- Heated/Cooled Diving/Swimmer Delivery Vehicle Suit (Code 32)

### Phase II completed (June 2013)

- Compact Device for Quantitative Measurement of In-vivo Gas Bubble Formation

## Future Topics

- High Efficiency CO<sub>2</sub> Absorbers for Re-breathers
- Improved DISSUB Gas Sensors
- 3D-SONAR Integrated Into a Diving Helmet Heads-up Display
- Biometric Monitoring Via a Dive Watch
- Contaminated Water Mitigation Garments
- Hyperbaric Ultrasound Device for DISSUB





# FY 15 Submission Process



- **General Submission Info**

- Check our Broad Agency Announcement (BAA) page
- Anyone can submit to the ONR Long Range BAA
  - <http://www.onr.navy.mil/en/Contracts-Grants.aspx>
- Rolling submission throughout fiscal year

- **FY15 Pre-proposal (White Paper) Review Process**

- **Pre-proposal due NLT 27 August**
- No more than 2-4 pages (request template by email)

- **Full Proposal Invitations**

- **Announced NLT 10 September**
- Submit to Grants.gov (universities, non-profits)
  - <http://www.grants.gov/>
  - SF 424 Block 4: Enter "ONR 342 – D'Angelo"
- **Full Proposal due NLT 15 October**
  - With Animal/Human use approval



# ONR Expenditure Requirements



- **Proper financial planning important up front**
  - Monthly spend plan to meet ONR expenditure benchmarks
- **Work with your financial office and ONR**
  - **Periodic & on-time billing essential**
- **Benchmarks (Grant funding lasts for two years)**
  - First Year Execution
    - NLT March 20%
    - NLT September 56%
  - Second Year Execution
    - NLT March 81%
  - **Failure to meet the benchmarks may jeopardize future years funding**



# Expectations



- **Communication – have a story for your project**
  - Progress reports – tell ONR all the good things you are doing!
    - Some reporting mandatory for contracts
  - Annual and Final reports required
  - Publications – the coin of the realm!
    - High impact factor, peer-reviewed journals – we count!
    - Submit PDFs to ONR and the Defense Technical Information Center (DTIC); <http://www.dtic.mil/dtic/submit/>
- **Annual Program Review**
  - Chance for the community to get together
  - Formal review of investments for Customers and Stakeholders
  - Expect to present your work and receive feedback
- **Transition Plan**
  - What is the end game for the Navy diver/submariner?
  - Application of findings?





## Other ONR Funding Opportunities



- **Basic and Applied Research Challenge (BRC & ARC)**
- **Multidisciplinary Research Program of the University Research Initiative (MURI)**
- **Defense University Research Instrumentation Program (DURIP)**
- **Young Investigator Program (YIP)**
- **Navy Small Business Technology Transfer (STTR) & Small Business Innovation Research (SBIR)**
- **ONR Global**
  - <http://www.onr.navy.mil/en/Science-Technology/ONR-Global.aspx>