Diving Effects of Excess CO_2 and O_2: Multiomic Characterization of Physiological Responses to Hyperbaric Hypercapnic Hyperoxia

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Disclosures

- The views expressed in this presentation are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government.
- The presenter has no conflicts of interest.
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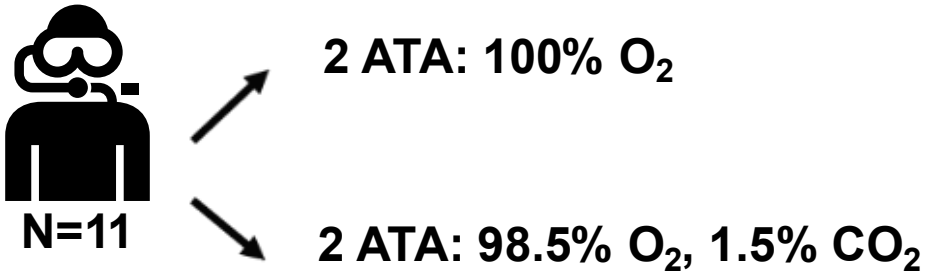
- The study protocol was approved by the Naval Submarine Medical Research Laboratory Institutional Review Board (NSMRL.2023.0005) in compliance with all applicable federal regulations governing the protection of human subjects.

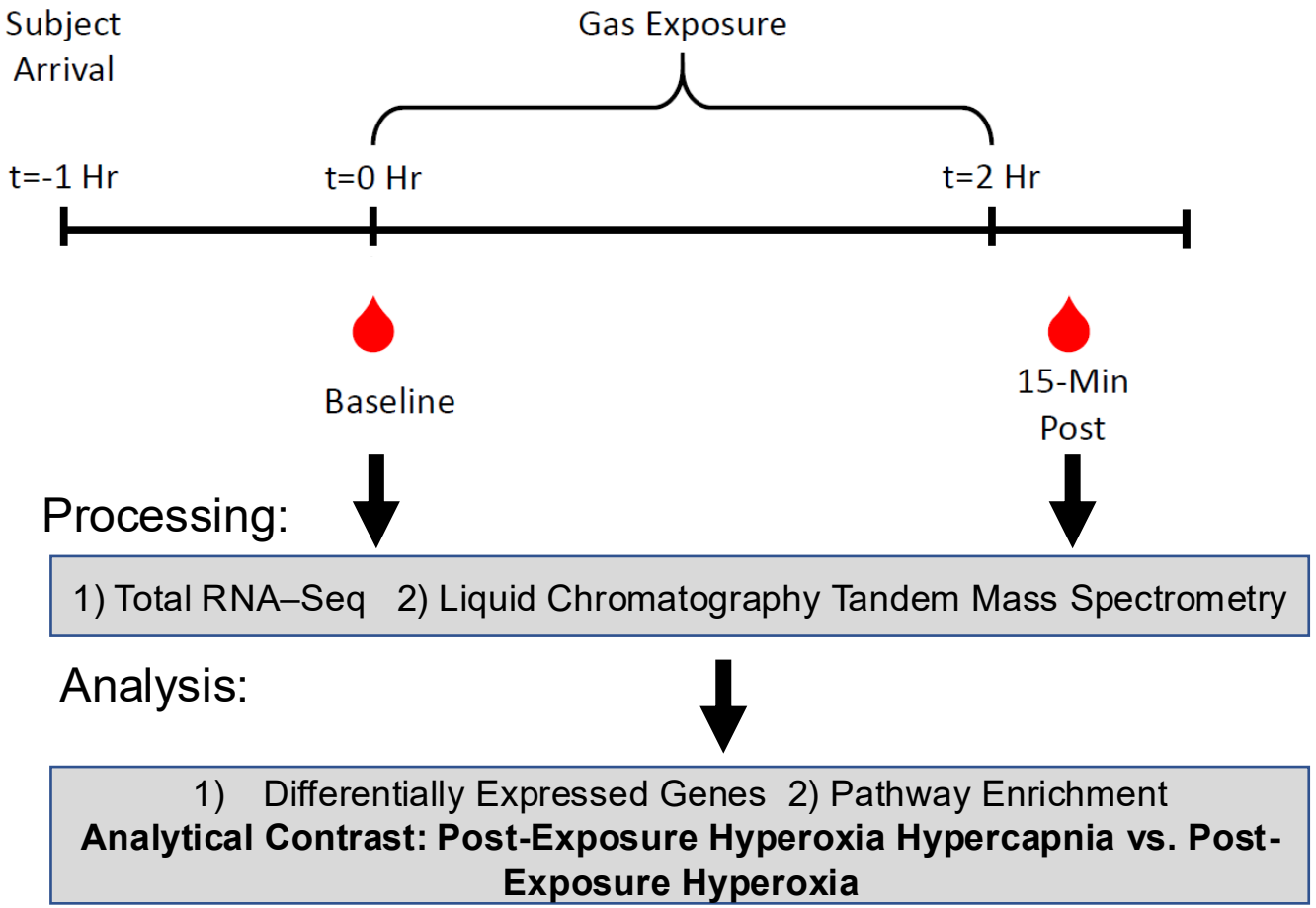
Hazard: Hypercapnic Hyperoxia

Insidious Onset | Incapacitating | Narrows Operational Envelopes

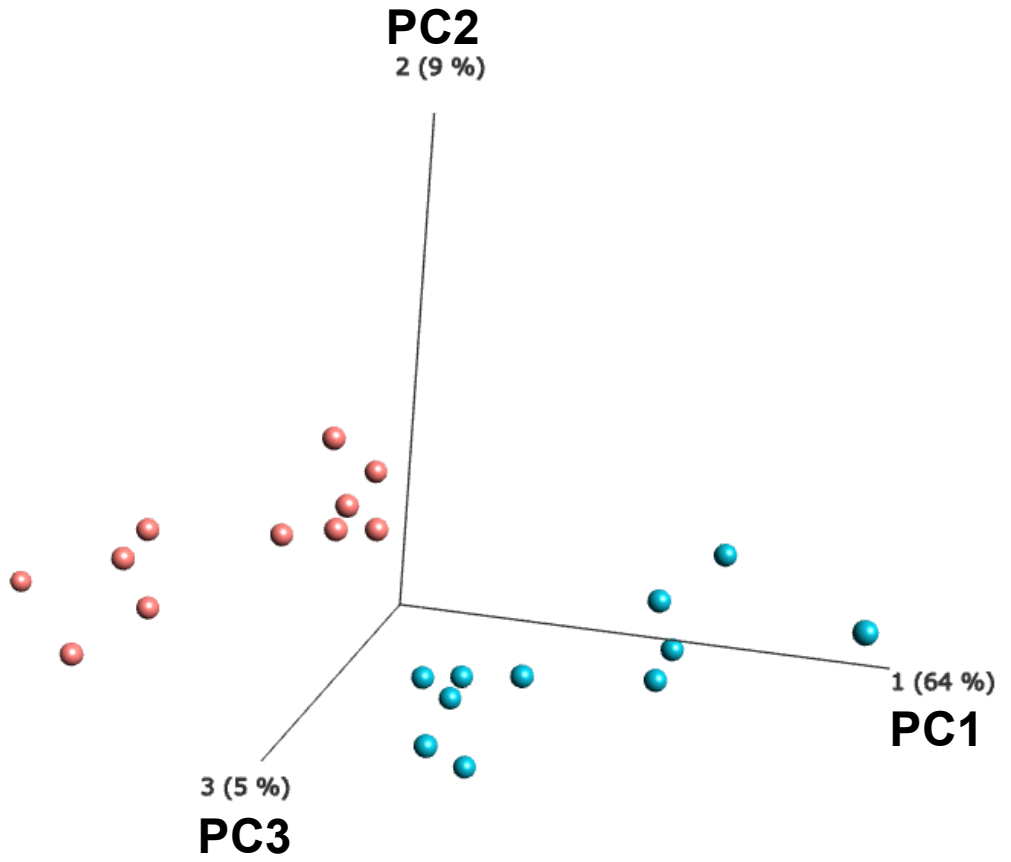
U.S. Navy Photos

Study Design & Methods





Global Proteomic Shift



Hypercapnic hyperoxia elicits a distinct physiological response measurable in the acute post-exposure window

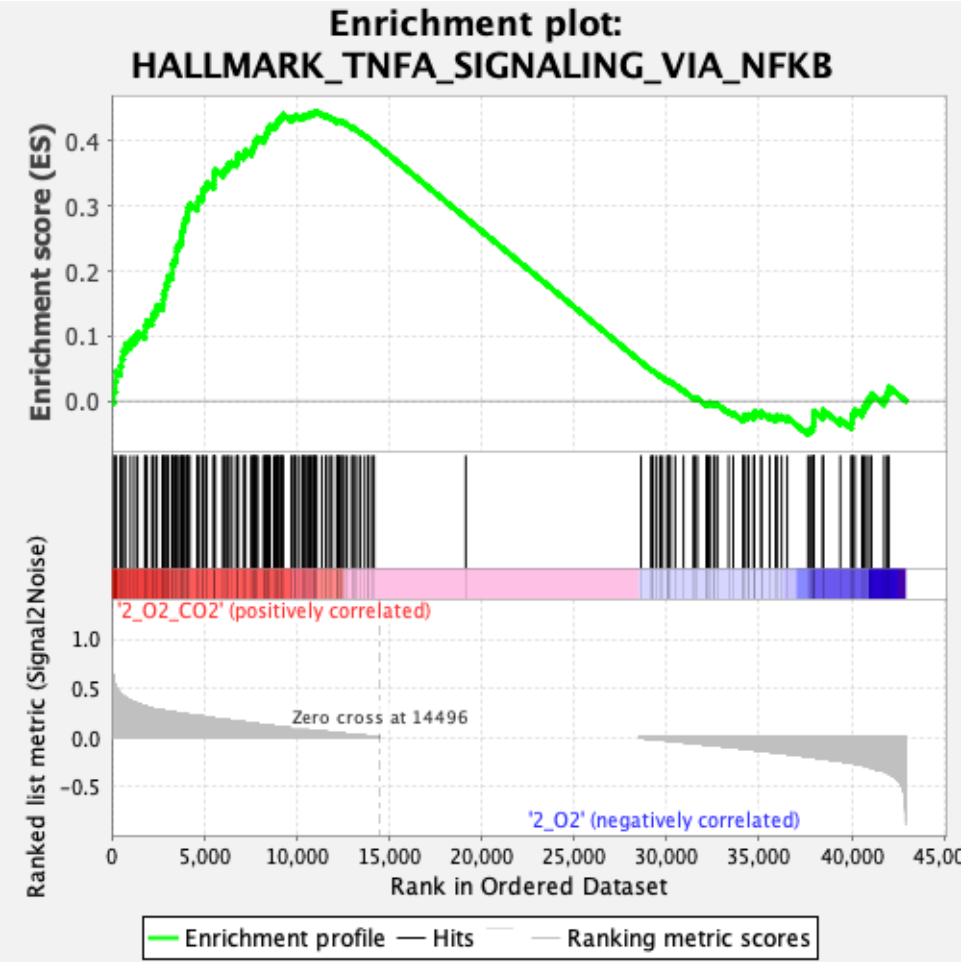
Suppression of GIMAP-Associated Transcripts

Gene Symbol	Adjusted p-value (FDR)	Function
GIMAP8	4.0 x 10^-5	Immune Cell Survival
GIMAP7	4.0 x 10^-5	Regulates T-cells
ADGRG7	4.0 x 10^-5	Cell adhesion receptor
ENSG00000267904	4.0 x 10^-5	Regulatory non-coding RNA
ENSG00000291221	4.0 x 10^-5	Regulatory non-coding RNA

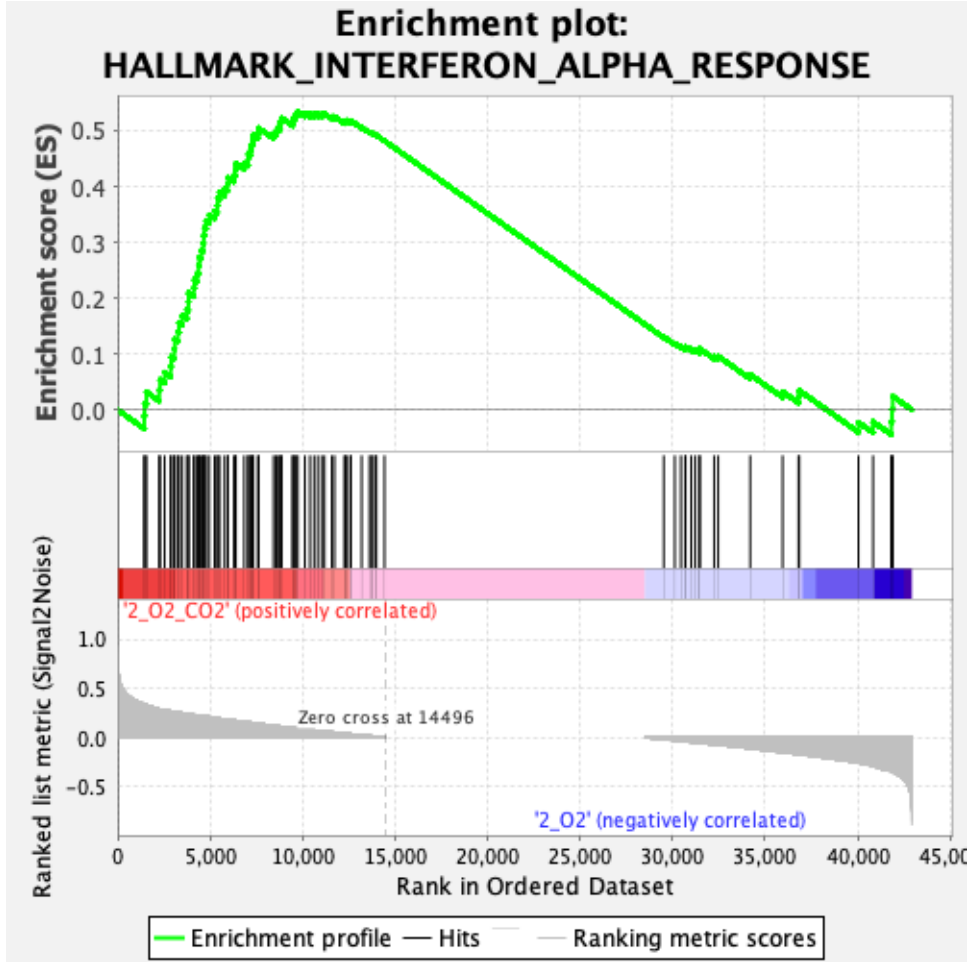
Targeted dropout of specific leukocyte-associated transcripts.

GIMAP: GTPase IMAP Family Member; ADGRG7: Adhesion G Protein-Coupled Receptor G7; FDR: False Discovery Rate

Transcriptional Activation of Inflammatory Pathways



FDR q = 0.044, **NES**= 1.52

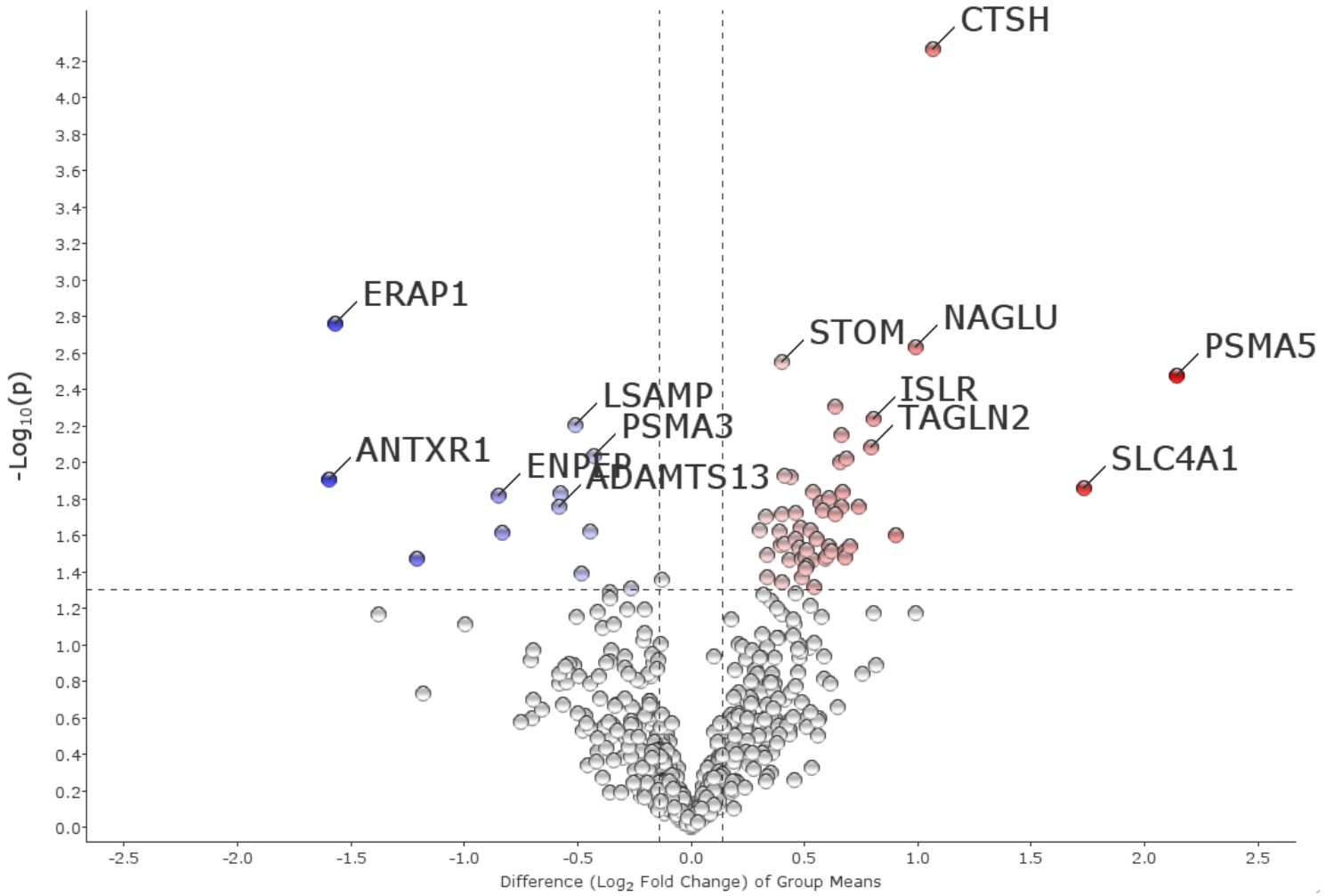


FDR q = 0.008, **NES**= 1.69

GSEA reveals coordinated upregulation of innate immune pathways (Interferon-α, TNF-α)

GSEA: Gene Set Enrichment Analysis; IFN-α: Interferon-Alpha; NES: Normalized Enrichment Score; TNF-α: Tumor Necrosis Factor-Alpha

Systemic Proteomic Alterations Following Exposure



Abundance changes indicate a mixed acute response: rapid effector mobilization and early acute-phase translation

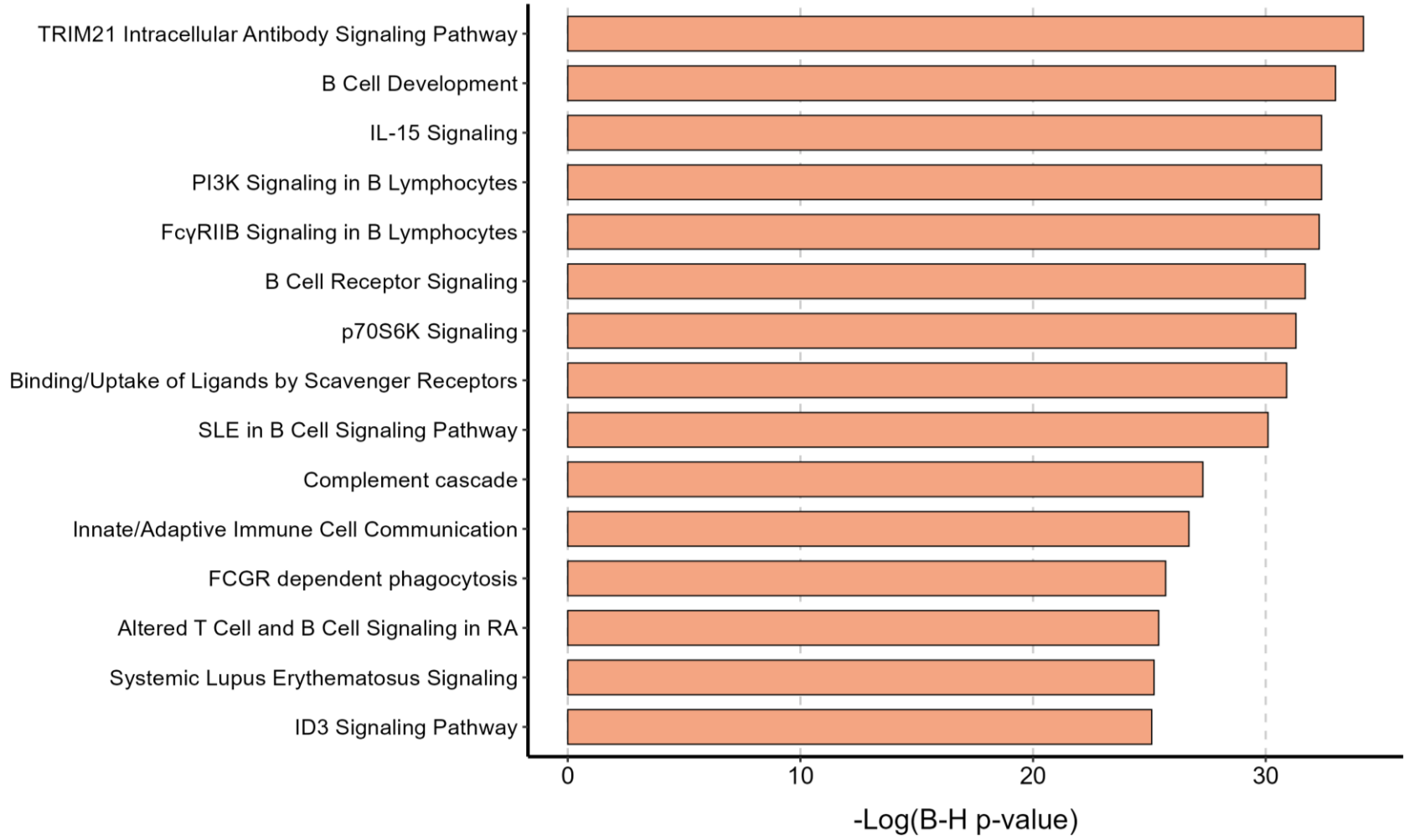
Isolating the Proteomic Signal

Strict FDR Correction q <0.05
Cathepsin H (CTSH)

Exploratory Threshold (p < 0.05)
67 Abundant Proteins

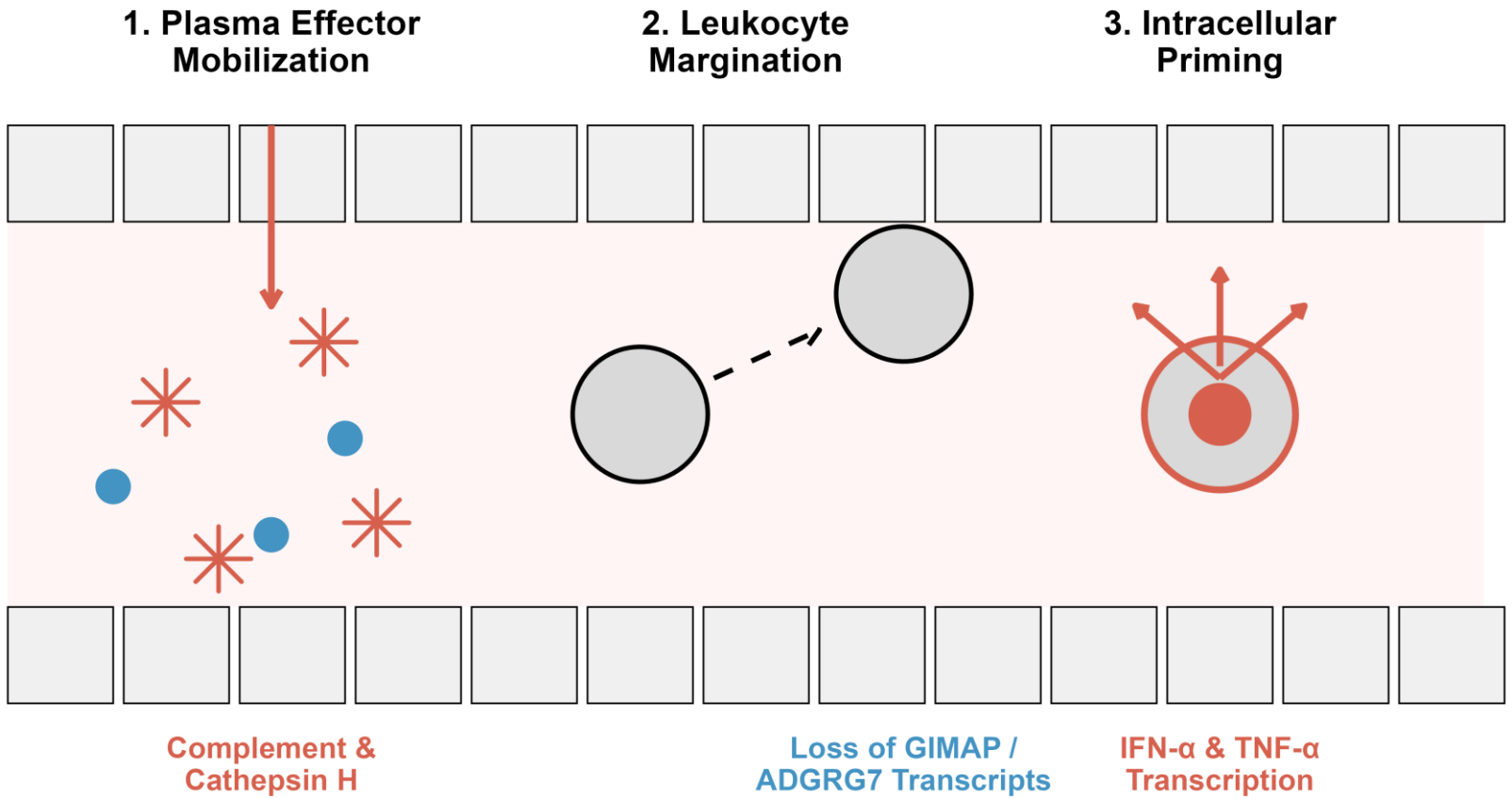
While CTSH is the sole target using a strict FDR, the broader 67-protein network maps to coordinated immune effector cascades

Activation of Immune Effector Cascades



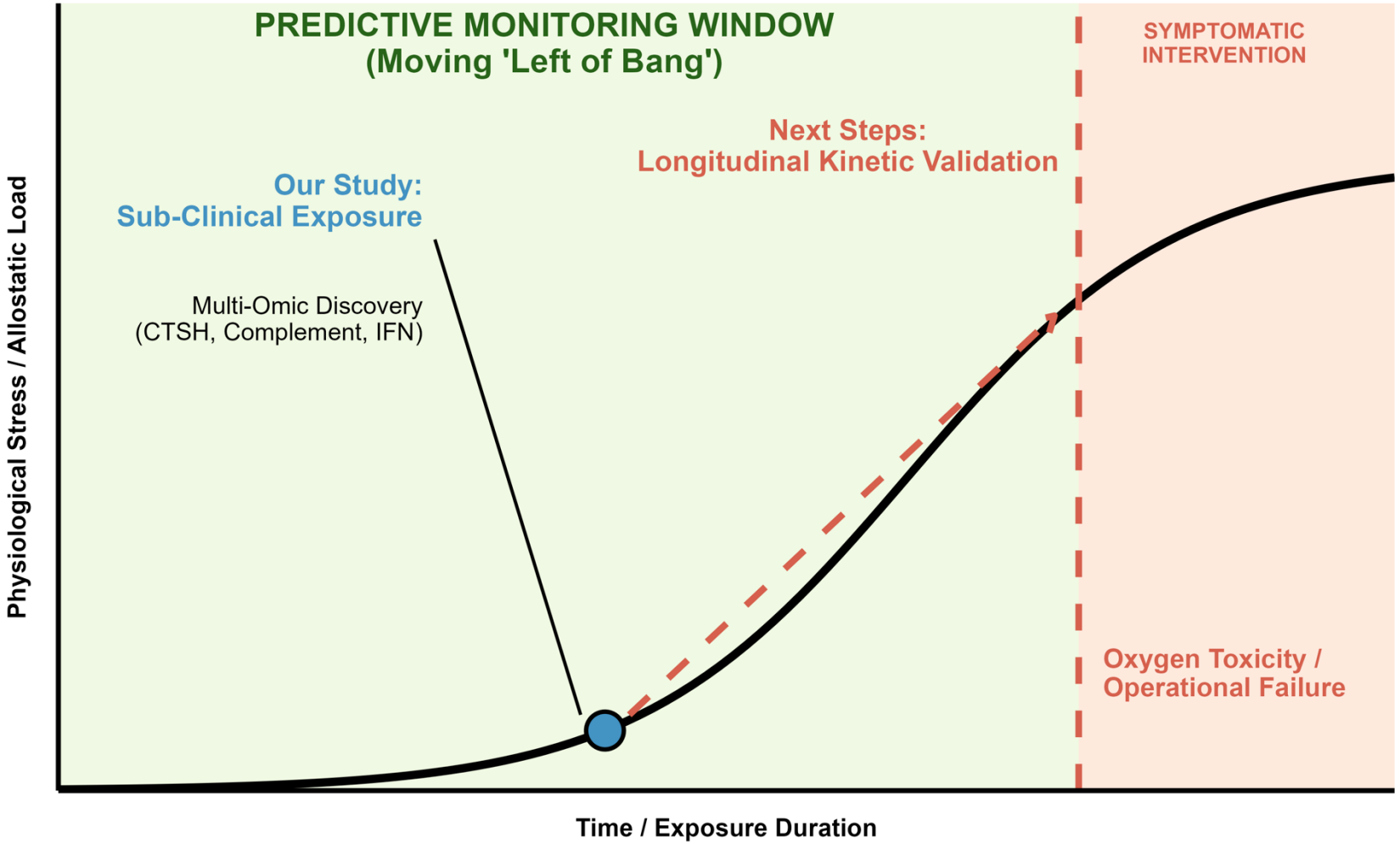
Pathway analysis reveals a highly significant, directional activation of B-cell signaling, TRIM21, and the complement cascade

Mechanistic Model of Acute Exposure



Hypercapnic hyperoxia appears to trigger a tri-partite acute response: plasma effector mobilization, leukocyte margination, and intracellular inflammatory priming

Limitations and Operational Translation



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