Learning from Whales: Identifying key genes in genetic pathway responses to low oxygen

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Background

- Oxygen levels are declining in warming oceans, posing challenges for marine life
- Marine mammals tolerate oxygen scarcity (hypoxia) during their dives, making them a great model to understand the low oxygen response
- Responses to hypoxic conditions in early eukaryotes include physically moving away (cell motility) or reducing metabolic rate
- The stress response may also play a role in affecting the hypoxia response

How do cell motility, stress, and metabolism interact with the hypoxia response?

Methods

Data sourcing:
• Gene sets of hypoxia and glucocorticoid pulled from the Molecular Signature Database (MSigDB)

Analysis:
• Gene regulatory networks created using the Cytoscape framework with GeneMANIA application (Shannon et al., 2003)

RNA-sequencing:
• Human, dolphin, pilot whale, humpback whale, sperm whale, and beaked whale cells exposed to +/- hypoxia/cortisol
• Gene expression quantified with RNAseq

Results

Do these three genetic responses help tolerate low-oxygen conditions?

Cell Motility

Evidence for coupling of the hypoxia and cell motility pathways in early eukaryotic evolution
• PGK1 and GSK3 are co-expressed even in non-motile yeast

Metabolism

The most genes present are used for anaerobic respiration
• Glycolysis is overrepresented, with 337 genes in the genome

Stress Hormones

Adding cortisol to beaked whale cell cultures suppressed the hypoxia response
• Tested in Pck1, G6pc, Per1, SGK1, and Igfbp1 (known GR downstream targets)

Takeaways and Applications

Marine Mammal Conservation
• Knowing how stress reduces low oxygen response in marine mammals can guide policy regulating anthropogenic stressors

Applications to human health
• Could provide insight into ways humans cope with low oxygen conditions in medicine, such as strokes or cardiac arrest

References:

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