Apr 28th, 12:00 AM - 12:00 AM

Hypobaria and Hypoxia Exert Separate Effects on HIF Expression in Drosophila melanogaster

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Senior Scholars Day

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Introduction: Global surface temperatures have been rising alarmingly over recent centuries due to anthropogenic greenhouse gas emissions. Some of the largest temperature effects have been found at the poles and in mountain regions such as the Himalayas where new higher altitude habitat is potentially available for insect populations. While other studies have examined low oxygen effects on development, we are aware of none that have examined the effects of low pressure; low levels of oxygen (hypoxia) typically stimulate the adaptive expression of hypoxia inducible factor genes (HIFs).

Methods: Using a self-built hypobaric chamber, we exposed newly emerged fruit flies (*Drosophila melanogaster*) to a simulated altitude of 5,500m ASL where atmospheric pressure is 50% of that of sea level (hypobaria). Expression of the yolk-protein receptor *yolkless*, and the insulin-receptor substrate protein *chico* (as measured by Real Time-PCR) was suppressed at high altitudes. However, exposure to simulated high altitude unexpectedly suppressed ovarian and female whole-body expression of the HIF gene SIMA-A indicating that the effects of low levels of oxygen and low pressure may be separate. To tease these effects apart, we used a high-oxygen gas mixture at low pressure to simulate the effect of a sea-level oxygen levels at high altitude on SIMA production. Similarly, we used a 10% oxygen mix at normal pressure to compare gene expression against air at high altitude.

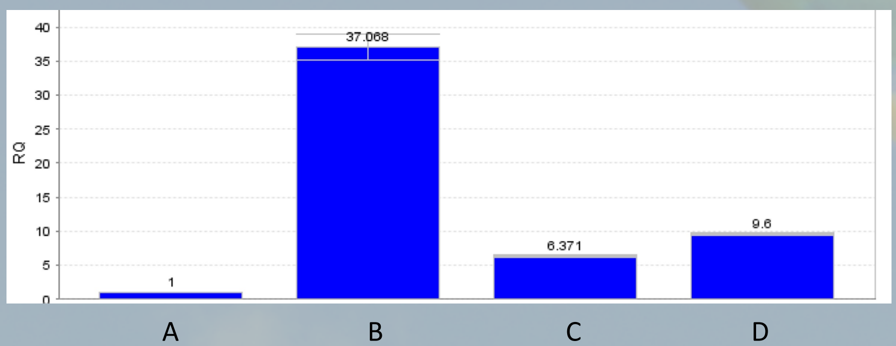

Figure 1: The separate effects of low pressure and low oxygen concentrations on the expression of SIMA-A hypoxia inducible factor in *Drosophila melanogaster* as measured by Real-Time PCR. A: 50% of normal atmospheric pressure/normal O_2 availability, B: 100% pressure/half normal O_2 availability; C: 50% pressure/half normal O_2; D: 100% pressure/normal O_2 availability.

Results: Figure 1 demonstrates that hypoxia and hypobaria may indeed exert separate effects on the expression of SIMA-A

- Compare A v D- Low pressure leads to suppression of SIMA production at normal O_2 levels (novel observation)
- Compare A v C- Low O_2 at Low pressure leads to elevated SIMA (expected).
- Compare B v D- Low O_2 at normal pressure leads to elevated SIMA (expected).
- Compare B v C- Low pressure leads to lower SIMA production than normal pressure at low O_2. (novel observation)

Taken together, these data indicate that there may be a novel pressure-sensing system in flies that is separate from the hypoxia sensing systems (HIFs/ HIF-prolyl-hydroxylases) that would normally regulate responses to low levels of oxygen availability. The nature of this novel mechanism is under investigation but we are unaware of any being reported in the literature in any organism to date.

Future studies

- Tissue-specific expression of the HIF using confocal examination of GFP-tagged SIMA construct fly lines.
- Experiments to determine the effects of long-term exposure to high altitude. While not technically possible in a laboratory, preliminary work with the Nepali Department of Agriculture is underway for a long-term study at Lobuche (5200m) in the Everest region.