**Transcriptome response to high-altitude exercise in Andean Highlanders with Chronic Mountain Sickness before and after hemodilution**

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Chronic Mountain Sickness (CMS), a disease common among highlanders, is characterized by excessive production of red blood cells, pulmonary hypertension, and exercise intolerance. While little is known about pathways leading to CMS, hemodilution has been anecdotally reported to alleviate CMS symptoms. To better understand the transcriptomic profile of CMS and the impact of isovolemic hemodilution, we collected blood samples before and after acute VO2max exercise from Andean male highlanders (~4300 m) with (n = 6) and without (n = 8) CMS (both pre- and post-hemodilution). Differentially expressed genes were selected based on transcriptomic differences in each group. Upregulation of inflammatory pathways (Neuroinflammation, IL-8, Natural Killer Cell signaling), Cardiac Hypertrophy, and Cdc42signaling were noted among CMS subjects before hemodilution, including notable changes in *IRAK3, IRAK4*, *HMOX1, IFNGR2, and IL6R* genes. The upregulation of various inflammation and pulmonary hypertrophy pathways detected in CMS subjects pre-hemodilution shifted to a pattern more similar to control subjects following hemodilution.