Title: The human Golgi anti-apoptotic protein promotes cell invasion by an H_2O_2-dependent mechanism

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Abstract: The human Golgi anti-apoptotic protein (hGAAP) is a novel highly conserved Golgi-localized cation channel that modulates Ca^{2+} fluxes from the intracellular stores, inhibits apoptosis and increases cell motility via a SOCE-dependent calpain2 activation that increases focal adhesions turnover. GAAP is expressed in all human tissues and is considered a housekeeping gene. Bioinformatics analyses suggest a link between dysregulation of hGAAP expression and several human cancers.
Unpublished data indicate that hGAAP overexpression increases *in vitro* and *in vivo* cell invasion, extracellular proteolytic and specifically MMP2. Conversely, hGAAP KD by siRNA reduces cell invasion and MMP2 activity, while the overexpression of an hGAAP null mutant has no effect on cell invasion or proteolytic degradation. Moreover, the overexpression of hGAAP results in the accumulation of intracellular ROS levels (CellROX) and specifically of H2O2 (HyPerRed). The reduction of both hGAAP-induced *in vitro* cell invasion and extracellular proteolytic degradation upon catalase addition indicates that H2O2 plays a role in this mechanism. A deeper understanding of hGAAP impact on cell invasion might contribute to provide new insights into the complex mechanisms related to Ca2+ and ROS signalling involved in cell invasion.

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