Porcù et al. demonstrated that Annexin A2 (ANXA2) is a pivotal mediator of the pro-oncogenic features displayed by glioblastoma (Glioblastoma) tumors, the deadliest adult brain malignancies, being involved in the cell stemness, proliferation, and invasion, thus negatively impacting patient prognosis. Based on these results, they hypothesized that compounds able to revert ANXA2-dependent transcriptional features could be exploited as reliable treatments to inhibit Glioblastoma cell aggressiveness by hampering their proliferative and migratory potential. Transcriptional signatures obtained by the modulation of ANXA2 activity/levels were functionally mapped through the QUADrATiC bioinformatic tool for compound identification. Selected compounds were screened by cell proliferation and migration assays in primary Glioblastoma cells, and we identified Homoharringtonine (HHT) as a potent inhibitor of Glioblastoma cell motility and proliferation, without affecting their viability. Further molecular characterization of the effects displayed by HHT, confirmed its ability to inhibit a transcriptional program involved in cell migration and invasion. Moreover, they demonstrated that the multiple antitumoral effects displayed by HHT are correlated to the inhibition of PDGFRA-dependent intracellular signaling through the impairment of STAT3 and RhoA axes. The results demonstrate that HHT may act as a potent inhibitor of cancer cell proliferation and invasion in glioblastoma, by hampering multiple PDGFRα-dependent oncogenic signals transduced through the STAT3 and RhoA intracellular components, finally suggesting its potential transferability for achieving an effective impairment of peculiar Glioblastoma hallmarks [1)].

1)
Porcù E, Maule F, Manfreda L, Mariotto E, Bresolin S, Cani A, Bortolozzi R, Puppa AD, Corallo D, Viola G, Rampazzo E, Persano L. Identification of Homoharringtonine as a potent inhibitor of glioblastoma cell proliferation and migration. Transl Res. 2022 Jul 1:S1931-5244(22)00151-7. doi: 10.1016/j.trsl.2022.06.017. Epub ahead of print. PMID: 35788055.