

## Transcriptional regulation of myeloid-derived suppressor cell development in neoplasia

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Myeloid-derived suppressor cells (MDSC) comprise immature myeloid populations produced in diverse pathologies, including neoplasia. Because of their ability to block antitumor immunity and support angiogenesis, MDSC have emerged as a significant opponent to cancer therapy. Despite this formidable consideration, the molecular basis of MDSC development remains incomplete. Thus, our laboratory has focused on how MDSC develop in the first place. We have been testing the central hypothesis that MDSC develop as a consequence of tumor-induced down regulation of interferon regulatory factor-8 (IRF8), a key myeloid developmental transcription factor. The importance of IRF8 in myeloid biology was originally unveiled in IRF8-deficient mice which develop myeloproliferative phenotypes. Altogether, our work reveals that MDSC form as a result of tumor-mediated down regulation of interferon regulatory factor-8. Moreover, IRF-8 down regulation could be facilitated by tumor-derived myelopoietic growth factors, such as G-CSF or GM-CSF which are known to activate STAT3 or STAT5 pathways, respectively. These findings not only identify IRF-8 as a potentially new downstream target of STAT3 or STAT5 activation, but also illuminate a previously un-described pathway of MDSC development that converges at the level of IRF-8 regulation. The identification of this new axis in MDSC-tumor biology has important implications for novel STAT- or IRF8-based clinical interventions during immune surveillance or immunotherapy.

### Biography

Abrams earned his Ph.D. degree from Indiana University and then completed a postdoctoral fellowship at Washington University. He is currently an Associate Professor at Roswell Park Cancer Institute. Prior to joining Roswell, Abrams served as an Investigator at the National Cancer Institute, NIH. He received several NIH Federal Technology Transfer Awards for the identification of human T cell peptide epitopes reflecting ras codon 12 mutations. Patents for these discoveries are issued both in the USA and Europe. He serves as a reviewer on study sections and has authored or co-authored nearly 90 articles, reviews and book chapters.

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