Eugen Dhimolea, Ph.D.

Positions:
Assistant Professor, Department of Molecular Pharmacology
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Research interests:
Despite the advances in cancer treatment, administered therapeutics often fail to eradicate the tumor cells in patients. One key focus area for our lab is the biology of the tumor cells that persist (residual tumor) after the initial acute cytotoxic effect of treatment and represent a reservoir for the eventual relapse. The goal of our research program is to functionally dissect the cancer cell state transitions that enable their persistence to multiple treatments and prevent the curative outcome. Our previous work has demonstrated that post-treatment residual cancer cells evade drug-induced cytotoxicity by adopting a distinct cellular state of reversible dormancy. This molecular program in persistent cancer cells resembles the adaptive diapause in epiblast stem cells, a dormant stage of suspended development in pre-implantation embryos triggered by stress and associated with suppressed Myc activity and overall biosynthesis. We aim to identify the molecular mechanisms that allow the tumor cells to enter, survive during and exit this diapause-like dormant state. We are also interested on the molecular similarities and unifying principles across treatment-induced adaptive dormancy and other survival states of quiescence in nature, such as the paused pluripotency during embryonic development. To this end, we combine the use of versatile in vitro (e.g. 3D monotypic and heterotypic organoid cultures) and in vivo (subcutaneous, orthotopic, or patient-derived xenografts) cancer models with molecular and functional studies. This work can potentially lead to new classes of therapeutic interventions for cancer patients.

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NCI/NIH	Diapause-like adaptation of triple-negative breast cancer cells during chemotherapy treatment

Recent publications:
*Indicates corresponding authors

- Sheffer M, Lowry E, Beelen N, Borah M, Amara SN, Mader CC, Roth JA, Tsherniak A, Freeman SS, Dashevsky O, Gandolfi S, Bender S, Bryan JG, Zhu C, Wang L, Tariq I, Kamath GM, Simoes RM, **Dhimolea E**, Yu C, Hu Y, Dufva O, Giannakis M, Syrgkanis V, Fraenkel E, Golub T, Romee R, Mustjoki S, Culhane AC, Wieten L, Mitsiades CS. Genome-scale screens identify factors regulating tumor cell responses to natural killer cells. *Nat Genet.* 2021 Aug;53(8):1196-1206.
- Duy C, Li M, Teater M, Meydan C, Garrett-Bakelman FE, Lee TC, Chin CR, Durmaz C, Kawabata KC, **Dhimolea E**, Mitsiades CS, Doehner H, D'Andrea RJ, Becker MW, Paietta EM, Mason CE, Carroll M, Melnick AM. Chemotherapy Induces Senescence-Like Resilient Cells Capable of Initiating AML Recurrence. *Cancer Discov.* 2021 Jun;11(6):1542-1561.
- **Dhimolea E***, de Matos Simoes R, Kansara D, Al'Khafaji A, Bouyssou J, Weng X, Sharma S, Raja J, Awate P, Shirasaki R, Tang H, Glassner BJ, Liu Z, Gao D, Bryan J, Bender S, Roth J, Scheffer M, Jeselsohn R, Gray NS, Georgakoudi I, Vazquez F, Tsherniak A, Chen Y, Welm A, Duy C, Melnick A, Bartholdy B, Brown M, Culhane AC, Mitsiades CS*. An Embryonic Diapause-like Adaptation with Suppressed Myc Activity Enables Tumor Treatment Persistence. *Cancer Cell.* 2021 Feb 8;39(2):240-256.
- **Dhimolea E***, de Matos Simoes R, Kansara D, Weng X, Sharma S, Awate P, Liu Z, Gao D, Mitsiades N, Schwab JH, Chen Y, Jeselsohn R, Culhane AC, Brown M, Georgakoudi I, Mitsiades CS*. Pleiotropic Mechanisms Drive Endocrine Resistance in the Three-Dimensional Bone Microenvironment. *Cancer Res.* 2021 Jan 15;81(2):371-383.