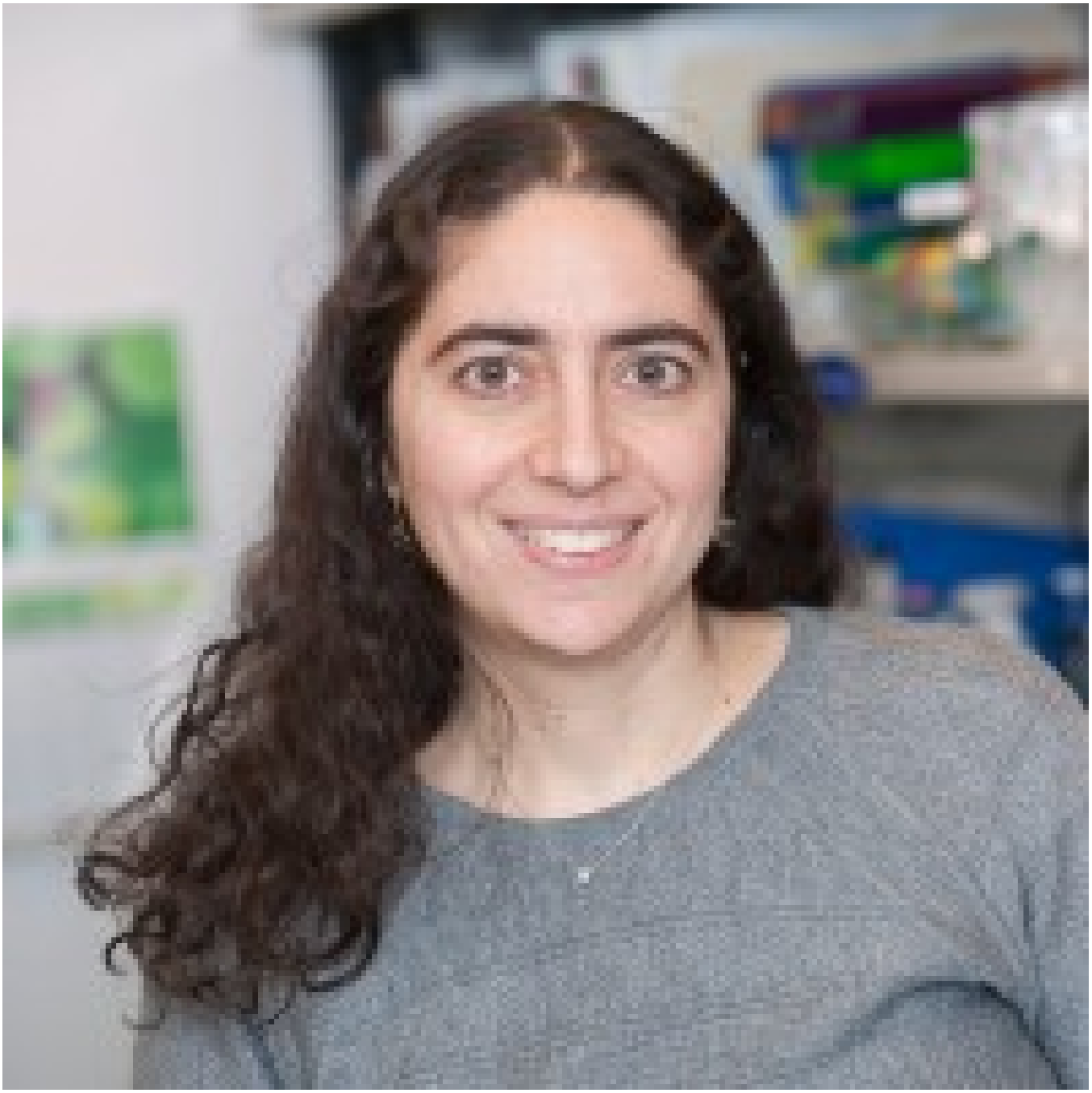
MEMORIAL HOSPITAL RESEARCH LABORATORIES

The Rona Yaeger Lab



Rona Yaeger, MD
Associate Attending Physician

Associate Professor

My laboratory and clinical research focus on understanding genomics and signaling in colorectal cancer to develop new treatments for patients. Colorectal tumors are characterized by a high level of baseline receptor tyrosine kinase (RTK) signaling. Oncogenic inhibition of these tumors, for example with RAS or BRAF inhibitors, releases these receptors from negative feedback suppression and attenuates response

to treatment. Combination treatment is thus needed, however, resistance often develops rapidly. Resistance alterations recurrently include gene amplifications that function to increase signaling from upstream RTKs despite presence of drug. Our lab uses cell lines, patient derived xenograft and organoid models, and clinical samples to evaluate tumor signaling and effects of drug inhibition. We are also analyzing the underlying processes driving resistance and investigating the role of chromosomal instability as an enabler of rapid resistance. Using novel agents and genomic techniques, we are testing the potential of inhibiting DNA repair pathways to prevent the emergence of resistance and prolong therapeutic responses.

Publications

1. Yaeger R, Mezzadra R, Sinopoli J, Bian Y, Marasco M, Kaplun E, Gao H, Zhao HY, Paula ADC, Zhu Y, Perez AC, Chadalavada K, Tse E, Chowdhry S, Bowker S, Chang Q, Qeriqi B, Weigelt B, Nanjangud GJ, Berger MF, Der-Torossian H, Anderes K, Socci ND, Shia J, Riely GJ, Murciano-Goroff YR, Li BT, Christensen JG, Reis-Filho JS, Solit DB, de Stanchina E, Lowe SW, Rosen N, Misale S. Molecular characterization of acquired resistance to KRAS(G12C)–EGFR inhibition in colorectal cancer. Cancer Discovery. 2023; 13: 41- 55.

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2. Chatila WK, Walch H, Hechtman JF, Moyer SM, Sgambati V, Faleck DM, Srivastava A, Tang L, Benhamida J, Ismailgeci D, Campos C, Wu F, Chang Q, Vakiani E, de Stanchina E, Weiser MR, Widmar M, Yantiss RK, Shah MA, Bass AJ, Stadler ZK, Katz LH, Mellinghoff IK, Sethi NS, Schultz N, Ganesh K, Kelsen D, Yaeger R. Integrated clinical and genomic analysis identifies driver events and molecular evolution of colitis-associated cancers. Nature Communications. 2023; 14:110.

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3. Rustgi N, Maria A, Toumbacaris N, Zhao H, Kargus K, Bryant M, Waksmundzki A, Aricescu I, Lefkowitz RA, Li BT, Chou J, Capanu M, de Stanchina E, Misale S, Shia J, Yaeger R. Combined RAF and MEK Inhibition to Treat Activated non-V600 BRAF Altered Advanced Cancers. The Oncologist. 2023; oyad247.

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4. Amodio V*, Yaeger R*, Arcella P*, Cancelliere C, Lamba S, Lorenzato A, Arena S, Montone M, Mussolin B, Bian Y, Whaley A, Pinnelli M, Murciano-Goroff YR, Vakiani E, Valeri N, Liao WL, Bhalkikar A, Thyparambil S, Zhao HY, de Stanchina E, Marsoni S, Siena S, Bertotti A, Trusolino L, Li BT, Rosen N, Di Nicolantonio F, Bardelli A, Misale S. EGFR blockade reverts resistance to KRAS(G12C) inhibition in colorectal cancer. Cancer Discovery. 2020; 10:1129-1139.

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5. Gao Y, Maria A, Na N, da Cruz Paula A, Gorelick AN, Hechtman JF, Carson J, Lefkowitz RA, Weigelt B, Taylor BS, Zhao HY, Reis-Filho JS, de Stanchina E, Rosen N, Yao Z, Yaeger R. V211D mutation in MEK1 causes resistance to MEK inhibitors in colon cancer. Cancer Discovery. 2019; 9:1182-1191.

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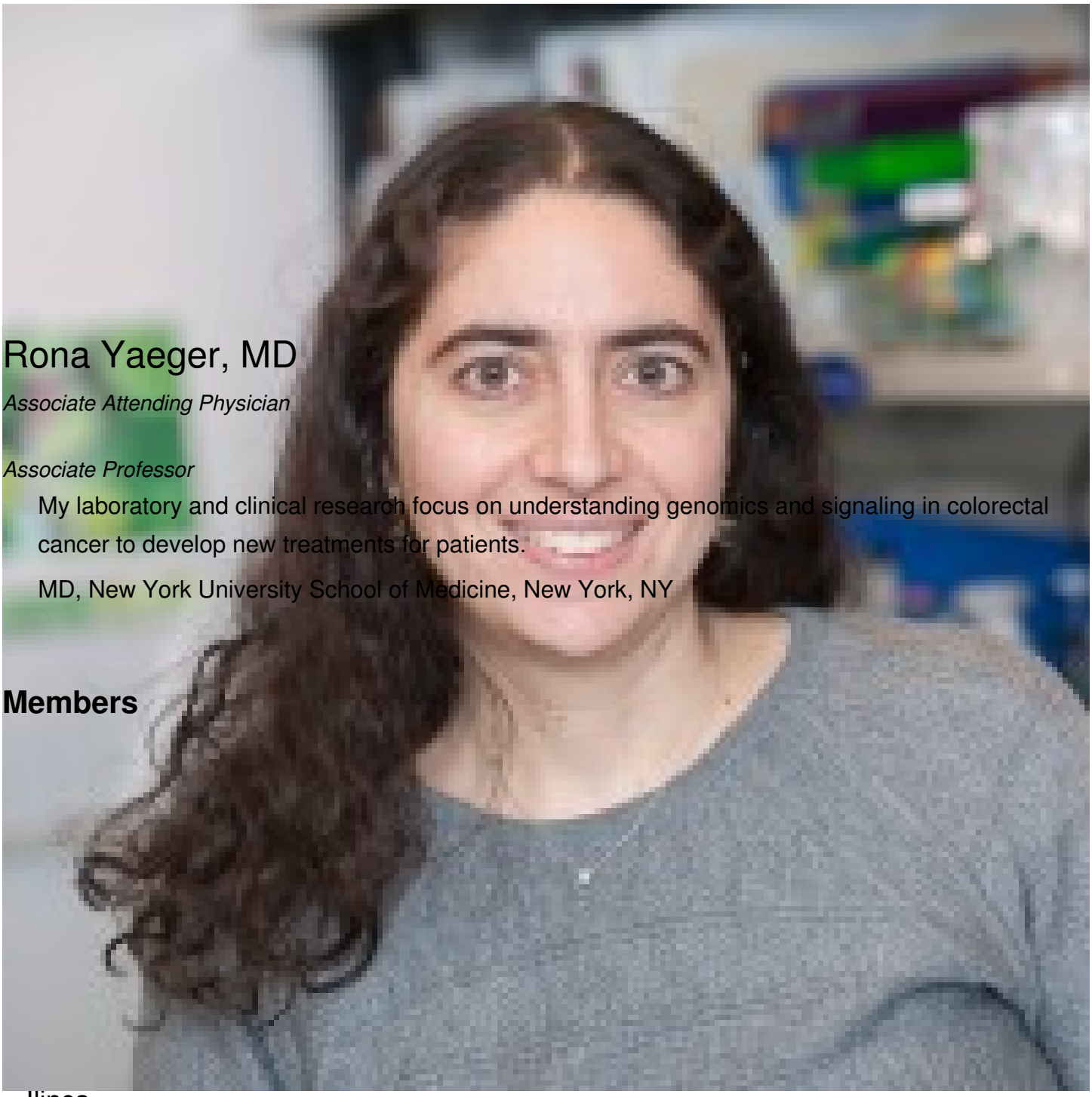
People



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MD, New York University School of Medicine, New York, NY

Members

Ilinca Aricescu

GSK Graduate Student

Lab Affiliations
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