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Titles & Department

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Specialization Areas

Cancer cell and molecular biology, DNA damage biology, Chemical biology.

Summary of Research & Work

Despite the established connections between ribosome biosynthesis and cancer growth, attempts to exploit Pol I as a clinically relevant drug target have been limited. Dr. Laiho and her team have discovered and characterized a family of novel small-molecules that potently and selectively inhibit Pol I transcription. These new molecular entities directly and specifically inhibit Pol I transcription. There are no comparators as other molecules classified as Pol I inhibitors act by targeting cellular topoisomerases. The highly innovative revelations by Dr. Laiho's team affirm that tumor cells are more dependent on ribosome biogenesis than normal cells and that therapeutic index is attainable.

The team uses unbiased, broad functional genomics and cancer cell line vulnerability screens and detailed mechanistic analyses to uncover biomarkers denoting sensitivity. These approaches facilitate the therapeutic use of Pol I inhibitors in the clinic and aid in identifying patients benefiting from this strategy. Their work is built on interdisciplinary expertise in cancer biology, drug discovery, development, and preclinical modeling and aims at clinical translation of these advances. This intellectual property is extensively covered with existing granted and pending patents.

Inventions, Patents & Copyrights

- Laiho M, Peltonen K. US 8,680,107; US 10,214,491; EU 2195316 (GB, FR, DE, ES, IT); EU 2889297 (GB, FR, DE, ES, IT, IR); Canada 2,691,227; Canada 2,912,456 "Activators and therapeutic applications thereof" 2016-2018. Total 6 granted patents.
- Laiho M, Barrow JA, Colis L, Ernst G, Sanders S. PCT/US2015/021699/15765295/2,943,022 US, EU, Canada "Compounds which inhibit RNA polymerase, compositions including such compounds, and their use" 2014-. 2 granted patents; EU 3119781 (GB, IR, FR, DE, ES, IT); US 11,001,581. 1 pending patent.
- Laiho M, Liu H, Sirajuddin P, Ikonen E. 16/335,737 EU, 17853955.7 US, "Combinatory treatment strategies of cancer based on RNA polymerase I inhibition" 2016-. Total 2 pending patents.
- Shah AA, Casciola-Rosen L, Rosen A, Igusa T, Laiho M. PCT/US2018/047770 "Screening Method to Identify Scleroderma Immune Responses with Anti-cancer Activity, and Induction of such Immune Responses for Cancer Therapy". 2 granted patents; US 11,454,630; EU 18849370.

- Laiho M, Barrow JA, Begum A, Fan W, Liu H, NV Rajesh Kumar, Stachelek G, de Leon P, Dorado T. PCT: 18/024,407 (US); 18/024,417 (US, EU); 18/024,421 (US); Compounds which inhibit RNA polymerase, compositions including such compounds, and their use.

Publications

- Peltonen K, Colis L, Liu H, Trivedi R, Moubarek MS, Moore HM, Bai B, Rudek MA, Bieberich CJ, Laiho M. A targeting modality for destruction of RNA polymerase I that possesses anticancer activity. **Cancer Cell** 25: 77-90, 2014.
- Jäämaa S, af Hällström TM, Sankila A, Rantanen V, Koistinen H, Stenman U, Zhang Z, Yang Z, De Marzo A, Taari K, Ruutu M, Andersson LC, Laiho M. DNA damage recognition via activated ATM and p53 pathway in non-proliferating human prostate tissue. **Cancer Res.** 70: 8630-8641, 2010.
- Colis L, Ernst G, Sanders S, Liu H, Sirajuddin P, Peltonen K, DePasquale M, Barrow JC, Laiho M. Design, synthesis and structure-activity relationships of pyridoquinazoline-carboxamides as RNA polymerase I inhibitors. **J. Med. Chem.** 57: 4950-4961, 2014.
- Wei T, Najmi SM, Liu H, Peltonen K, Kucerova A, Schneider DA, Laiho M. Small-molecule Targeting of RNA Polymerase I Activates a Novel, Conserved Transcription Elongation Checkpoint. **Cell Reports** 23: 404-414, 2018.
- Fan W, Eklund E, Sherman RM, Liu H, Pitts S, Ford B, NV Rajeskumar, Laiho M. Widespread germline genetic heterogeneity of human ribosomal RNA genes. **RNA** 28(4):478-492, 2022.