A Cure for HIV? Consortium Meeting of HIV Cure Research at CHRP

On May 20th 2016, the California HIV/AIDS Research Program (CHRP) brought together CHRP-funded researchers who are working toward a cure for HIV, to share their results to date and help inform the way forward. Dr. Tom Hope from Northwestern University served as the moderator. Two senior scientists who serve on the CHRP Advisory Council, Drs. Barbara Shacklett from UC Davis and David Looney from UC San Diego, offered commentary and suggestions. Terry Cunningham and Bill Stewart, community representatives from the CHRP Advisory Council, also attended the meeting.

Nine CHRP-funded investigators presented their work, which included multiple presentations on aspects of retroviral latency and transcription, a new system to disrupt the HIV reservoir, and other topics. Below are key aspects reported by the investigators. Based on the robust discussion and practical suggestions offered, CHRP is considering a similar meeting in 2017.

- Emilie Battivelli from the Gladstone Institutes is investigating the role of t-cell activation in latency, and will identify the genes and cellular pathways that establish and maintain HIV latency in primary $CD4^+$ T cells.
- Daniele Boehm from the Gladstone Institutes is working with bromodomain proteins, and shared her successful discovery of the interactions between BRD2 and cyclin T1, between BRD8 and Tat, and the synergy between BRD inhibitors and SMYD inhibitors.
- Koh Fujinaga of UCSF is working to determine the molecular mechanism that regulates the transition/equilibrium between active P-TEFb and 7SKsnRNP. He showed previously uncharacterized HEXIM proteomes, and focused on the FET family of proteins.
- Britt Glaunsinger from UC Berkeley has analyzed the post-transcriptional modification state of individual RNAs at single nucleotide resolution, and has shown how a modification of 7SK (pseudouridylated at position U250) is critical to sequester HIV transcription factor P-TEFb.
- Dennis Hartigan-O'Connor at UC Davis is determining whether the functional cure of HIV is most easily achieved in the setting of relative memory CD4+ T cell deficiency – having implications for a cure at the early reservoir stage vs the reservoir established during long-term infection.
- Masakazu Kamata from UCLA presented his work toward reprogramming HIV-specific exhausted T cells to become naive T cells, which can then develop into functional memory T cells.
- Nick Llewellyn from USC has developed several CRISPRs to disrupt latently infected cells, and is working toward an all RNA nucleofection strategy.
- Gema Mendez-Lagares at UC Davis is examining microbiota effects on Th17/Treg axis, and testing the likelihood of achieving cure in individuals that have developed immune systems polarized more highly to (i) Th17 cells or to (ii) T-reg cells using an "extreme groups" approach.
- Vladimir Pak showed that CDK11 activates HIV transcription and replication, and that the level of CDK11 in CD4+T cells is 20 times lower than that in standard cell lines. Because of this, CDK11 may be a promising therapeutic target for discovery of new treatments for cancer, beyond the setting of HIV infection.

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The California HIV/AIDS Research Program (CHRP) fosters outstanding and innovative research that responds to the needs of all people of California, especially those who are often underserved, by accelerating progress in prevention, education, care, treatment, and a cure for HIV/AIDS. CHRP was founded by the California state legislature in 1983 to respond to the HIV/AIDS crisis in the state. Since the program began, CHRP has funded more than 2,000 research projects and distributed and monitored more than $275 million in state funds for HIV/AIDS research.

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