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Positions:
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Research interests:

Keywords: Human eye organoids, modeling of human eye diseases, live cell imaging of protein-chromatin interactions, eye diseases caused by mutations in PAX6, SOX2, and MAF genes, ATP-dependent chromatin remodeling BAF complexes, super-resolution microscopy, tissue engineering, multi –omics approaches and computational biology.

Mammalian eye development represents an advantageous system to understand the cellular, molecular, genetic and epigenetic mechanisms governing formation of new cell types, cellular differentiation, tissue-specific gene control, dynamic changes in the chromatin landscape, and subnuclear organization of chromatin. Differentiation of human pluripotent stem cells into various ocular cell types, including the cornea, lens, cone and rod photoreceptors, retinal progenitor cells, retinal pigmented epithelium, and retinal ganglion cells, enables studies of self-organization, interaction of DNA-binding transcription factors with chromatin at single cell and single molecule levels, generates models for cell replacement therapies and for tissue regeneration using endogenous adult stem cells. Importantly, genome engineering of isogenic human iPS cells using CRISPR-Cas9 technologies facilitates modeling of human ocular genetic diseases and provides opportunities for their therapies. For example, our ongoing studies are aimed to generate isogenic iPS cell lines carrying heterozygous and homozygous missense and nonsense mutations in transcription factor *PAX6*, the master regulatory gene of eye development. These studies model human aniridia and provide novel mechanistic insights into gene regulatory networks (GRNs) controlled by PAX6 in various ocular cell types.

Current grant funding:

R01 EY012200 (Cvekl, PI) (NIH/NEI)	01/01/2000 – 04/30/2022 Pax6 as a key regulator of lens development
R01 EY014237 (Cvekl, PI) (NIH/NEI)	04/01/2003 – 04/30/2025 Developmental regulation of lens gene expression

Recent publications (selected):

1. Yang, C., Y. Yang, L. Brennan, E.E. Bouhassira, M. Kantorow and **A. Cvekl**. 2010. Efficient generation of lens progenitor cells and lentoid bodies from human embryonic stem cells in chemically defined conditions. FASEB J. **24:**3274-3283.
2. Wolf, L., W. Harrison, H. Jie, Q. Xie, N. Xiao, J. Sun, L. Kong, S. A. Lachke, M.R. Kuracha, V. Govindarajan, P.K. Brindle, R. Ashery-Padan, D. C. Beebe, P.A. Overbeek, and **A. Cvekl.** 2013. Histone modifications and cell fate determination: Lens induction requires the lysine acetyltransferases CBP and p300. 2013. Nucleic Acids Res. **41:**10199-10214.
3. Sun, J., S. Rockowitz, Q. Xie, D. Zheng, and **A. Cvekl**. 2015. Identification of *in vivo* DNA-binding mechanisms of Pax6 and reconstruction of Pax6-dependent gene regulatory networks during forebrain and lens development. 2015. Nucleic Acids Res. 43:6827-6846.
4. Limi, S, A. Senecal, R. Coleman, M. Lopez-Jones, P. Guo, C. Polumbo, R.H. Singer, A.I. Skoultchi, and **A. Cvekl.** 2018. Transcriptional dynamics during lens fiber cell differentiation and novel insights into the denucleation process. J. Biol. Chem. **293**:13176-13190.
5. Kim S., A. Lowe, R. Dharmat, S. Lee, L.A. Owen, J. Wang, A. Shakoor, D.J. Morgan, A.A. Hejazi, Y. Li, **A. Cvekl**, M. DeAngelis, J. Zhou, R. Chen, and W. Liu. 2019. Generation, transcriptome profiling, and functional validation of cone-enriched human retinal organoids. Proc. Natl. Acad. Sci. U.S.A. **116:**10824-10833.