



Dr. Alicia Michael
Basel, Switzerland



2023 Finalist

How do transcription factors interpret and shape chromatin structure?

»The DNA in our cells is wrapped around histone proteins to form nucleosomes that package the DNA in the nucleus and regulates gene expression. This packaging physically "hides" the DNA from being accessed by transcription factors. While it has long been known in the field of epigenetics that transcription factors must be able to find and bind to their DNA binding motifs even when 'hidden' in chromatin, it was unknown how this was happening or what this looked like. During my postdoctoral work, we developed a method to test the binding of TFs throughout the nucleosome, enabling structure determination of the cellular reprogramming factors, OCT4 and SOX2 bound to their chromatinized motif. The structures reveal how, by recognizing just part of its DNA-binding motif, only a subset of OCT4's DNA-binding domains appears to hold the DNA, while SOX2 lifts the DNA away from the surface of the nucleosome. The structures informed our genomic studies to demonstrate that a partial DNA-binding motif engagement is sufficient for these factors to engage chromatin in cells. This may indicate how the transcription factors invade inactive regions of the genome and allow the recruitment of additional factors for DNA transcription and gene reactivation during cellular reprogramming.«

Dr. Alicia Michael

Postdoctoral Fellow (at the time of application)
at Friedrich Miescher Institute for Biomedical
Research Department Genome Regulation
Maulbeerstraße 66, 4057 Basel - Switzerland
E-Mail: aliciakmichael@gmail.com

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our Award finalist
Dr. Alicia Michael

