Sickle cell disease was the first identified molecular disease, one that has devastating clinical outcomes and affects nearly every organ system. This presentation will review more than 100 years of research and clinical care and provide a comprehensive view of a translational model that incorporates the full spectrum of translational research (discovery, basic, clinical, community application, and policy) to improve human health outcomes. The care of individuals with sickle cell disease also incorporates (a) investigators from diverse backgrounds working together on solutions, (b) a developmental framework, and (c) transformational change, all within a social context that has changed dramatically as well.