Award ID:
R1213

Project Title:
Recruitment of First-Time, Tenure-Track Faculty Members

Award Mechanism:
Recruitment of First-Time, Tenure-Track Faculty Members

Principal Investigator:
Cole, Francesca

Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Dr. Cole received her Ph. D. at Mount Sinai School of Medicine of New York University and her postdoctoral training at Memorial Sloan-Kettering Cancer Center. Her long-term goal is to gain a sophisticated mechanistic understanding of mammalian homologous recombination to improve cancer diagnostics and therapies.

As an undergraduate, Francesca Cole started her scientific career as a Sigma Xi Summer Research Fellow working on factors regulating mouse and human muscle cell differentiation in the laboratory of D. Stave Kohtz at Mount Sinai School of Medicine in New York. After the term of the fellowship, she continued to work in his laboratory while finishing her undergraduate degree at Hunter College of the City University of New York. She then received a prestigious Howard Hughes Medical Institute Predoctoral Fellowship and chose to study at MIT working in the laboratory of Leonard Guarente on aging in Saccharomyces cerevisiae. There she developed a deep and long-lasting appreciation for genetics. She improved techniques to isolate aged yeast and developed a screen for aging mutants. For family reasons, she moved back to New York where she joined the laboratory of Robert S. Krauss at Mount Sinai to complete her Ph. D. She studied the role of the Ig superfamily protein, CDO (pronounced “kiddo”), in mammalian myogenesis. She determined that CDO promotes myogenic bHLH transcription factors by a unique mechanism - inducing hyperphosphorylation of their obligate partners, the E proteins, reducing E protein homodimerization and favoring formation of the active myogenic bHLH – E protein complex. She generated two null mutant alleles of Cdo in the mouse and confirmed an in vivo role for CDO in promoting skeletal muscle development during embryogenesis. Intriguingly, she also discovered that mice lacking CDO showed the hallmark features of holoprosencephaly, a developmental defect of midline designation most often associated with mutation in Sonic hedgehog (SHH) pathway components. This work was the first to implicate that CDO acts to regulate the SHH pathway and pioneered studies that identified CDO and its related family member, BOC, as SHH co-receptors.

Francesca’s training as a developmental biologist and work on holoprosencephaly, a tragic and common developmental defect in humans, led to a desire to study meiotic recombination, errors in which are the leading cause of developmental disability in humans. She joined the laboratory of Maria Jasin at Memorial Sloan-Kettering Cancer Center where she worked in collaboration with Scott Keeney on mechanisms of meiotic recombination in the mouse. Using cytological and genetic methods, she determined that the meiotic recombination program is regulated progressively by homeostatic

mechanisms that are likely to suppress gamete aneuploidy. In Dr. Jasin's laboratory, she developed a determination to improve our general understanding of double-strand break repair by homologous recombination, defects in which lead to cancer. Frustrated with the molecular tools available to study mammalian recombination, she developed innovative technology and systems to probe homologous recombination at an unprecedented level of resolution. Her work enables the type of sophisticated analysis within a complex mammalian genome heretofore enjoyed only by more genetically tractable organisms, such as budding yeast. Armed with these new assay systems, she is poised to determine which homologous recombination pathways are prone to negatively impact genome integrity contributing to the etiology of cancer and improving cancer diagnostics. But, more importantly, she will determine how these pathways compensate and collaborate with one another, identifying targets that can be inhibited to treat cancer and improve cancer therapeutics.