MAR16-2015-020445

Abstract for an Invited Paper
for the MAR16 Meeting of
the American Physical Society

Monitoring of organ transplants through genomic analyses of circulating cell-free DNA.

IWIJN DE VLAMINCK, Cornell University

Solid-organ transplantation is the preferred treatment for patients with end-stage organ diseases, but complications due to infection and acute rejection undermine its long-term benefits. While clinicians strive to carefully monitor transplant patients, diagnostic options are currently limited. My colleagues and I in the lab of Stephen Quake have found that a combination of next-generation sequencing with a phenomenon called circulating cell-free DNA enables non-invasive diagnosis of both infection and rejection in transplantation. A substantial amount of small fragments of cell-free DNA circulate in blood that are the debris of dead cells. We discovered that donor specific DNA is released in circulation during injury to the transplant organ and we show that the proportion of donor DNA in plasma is predictive of acute rejection in heart and lung transplantation. We profiled viral and bacterial DNA sequences in plasma of transplant patients and discovered that the relative representation of different viruses and bacteria is informative of immunosuppression. This discovery suggested a novel biological measure of a person's immune strength, a finding that we have more recently confirmed via B-cell repertoire sequencing. Lastly, our studies highlight applications of shotgun sequencing of cell-free DNA in the broad, hypothesis free diagnosis of infection.