COMPUTATIONAL MEDICINE CENTER UNCOVERS NEW RNA CATEGORIES

THE INTERDISCIPLINARY EXPERTS OF JEFFERSON'S COMPUTATIONAL Medicine Center combine high-performance computing, data-driven hypothesis generation and wet laboratory work to unravel the biology and role of short RNA molecules with powerful regulatory roles. The Center's research is led by **Isidore Rigoutsos, PhD**, Richard H. Hevner Professor of Computational Medicine; **Yohei Kirino**, associate professor of biochemistry and molecular biology; and **Eric Londin, PhD**, assistant professor of pathology, anatomy and cell biology.

The group has uncovered new RNA categories and many previously unsuspected molecules that act as regulators. They have also demonstrated that the identity and abundance of these newly discovered regulators depend on a person's sex, population origin and ethnicity—as well as on tissue type, tissue state and disease.

For example, the team has shown that the size and specific sequence of fragments of transfer RNA (tRNA) depend on the kind of cancer cell in which they are found: in their studies, the same parental tRNA produced fragments that differed depending on whether they were in, for example, breast cancer or prostate cancer cells. When the researchers analyzed broader data from a group of 32 cancers, they found an array of complex relationships among tRNA fragments, messenger RNA (mRNA), proteins, genomic architecture, repetitive elements and the mitochondrion. The work suggested that tRNA fragments are as important as the full-length parental molecules; that they have extensive interconnections to gene templates and gene products that differ by disease type; and that these interconnections can be affected by a person's sex. The findings could provide new angles of attack specific to the type of disease and the sex of the patient.

The investigators' analysis further revealed that all 32 cancer types harbor essentially the same tRNA fragments and mRNA, but in very different abundances. Moreover, the fragments and the mRNA associate with each other in specific pairs that differ in each cancer. Surprisingly, even though the tRNA fragments partner with different mRNA in each cancer, these mRNA belong to the same core biological processes. The discovery suggests more ways in which cancers might differ from one another—and suggests that expression of the same gene can go awry differently in different cancer types. "These tRF-mRNA associations could provide valuable insights for how to approach research into treatment," Rigoutsos notes, "because they capture different relationships in every cancer." ■