Can gender play a role in determining cancer treatment choices?

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It is well known that men and women differ in terms of cancer susceptibility, survival and mortality, but exactly why this occurs at a molecular level has been poorly understood.

A study at The University of Texas MD Anderson Cancer Center reviewed 13 cancer types and provided a molecular understanding of sex effects in diverse cancers. The research revealed two cancer-type groups associated with cancer incidence and mortality, suggesting a "pressing need" to develop sex-specific therapeutic strategies for some cancers.

The research findings are published in the May 9 online issue of *Cancer Cell*.

Using data from The Cancer Genome Atlas, a team led by Han Liang, Ph.D., associate professor of Bioinformatics and Computational Biology, found more than half of the genes studied that were related to clinical practice of cancer treatment showed sex-biased signatures in certain cancer types.

"Our study helps elucidate the molecular basis for sex disparities in cancer and lays a critical foundation for the future development of precision cancer medicine that is sex-specific," said Liang. "This is a crucial finding as currently, male and female patients with many cancer types often are treated in a similar way without explicitly considering their gender."

Liang's group performed a comprehensive analysis of molecular differences between male and female patients, revealing two sex-effect groups associated with distinct incidence and mortality profiles and accounting for 53 percent of clinically actionable genes. Those genes are informative for clinical decisions and are either therapeutic targets or biomarkers that can help predict patient survival or tumor response.

In the study, Liang found one group contained a small number of sex-affected genes (weak group), while the other showed a much greater number of sex-biased molecular signatures (strong group). Liang said the current equal treatment of both genders may be appropriate for those in the "weak" group, but observations in the "strong" group are clinically significant.

"Special consideration should be given to those in the strong sex-effect group in terms of both drug development and practice," said Liang. "For a therapeutic target with a strong sex-biased signature, sex-specific clinical trials may be more likely to succeed. This new information is vital as the fundamental issue of sex differences for cancer prevention and therapy has not been investigated systematically."

Liang's team analyzed data in patient cohorts of 30 or greater samples for each sex for various cancers of the bladder, colon, kidney, brain, rectum, thyroid, liver and lung as well as acute myeloid leukemia. They looked for specific molecular data including somatic mutations, copy alterations, protein and gene expression and DNA methylation. The study included controls for other factors such as race, age, disease stage, smoking status and tumor purity.

"Interestingly, our analysis also suggested that sex bias might be amplified during the tumor formation process," said Liang. "However this observation should be interpreted with caution at this early stage as further efforts are needed to determine the relative contributions of

other factors, including tumorigenesis, sex chromosomes and hormones."

Provided by University of Texas M. D. Anderson Cancer Center