C-Path's Predictive Safety Testing Consortium Advances a Transformative Test to Detect Drug Induced Liver Injury

Serum Glutamate Dehydrogenase Activity Enables Sensitive and Specific Diagnosis of Hepatocellular Injury in Humans

TUCSON, Ariz., March 27, 2025 – Researchers from Critical Path Institute's® (C-Path) Predictive Safety Testing Consortium have proposed glutamate dehydrogenase (GLDH) as a more liver-specific biomarker for detecting liver injury, supporting clearer decision-making. Currently, alanine aminotransferase and aspartate aminotransferase (ALT and AST) are considered the "gold standard" biomarkers in clinical practice and drug development. However, these biomarkers are not specific to the liver and can reflect changes in other tissues, which may lead to unclear diagnoses, particularly in individuals with muscle conditions or muscle-related drug side effects. By contrast, GLDH offers greater specificity to the liver, addressing this critical limitation.

The team's initial studies showed that GLDH performed similarly to ALT for detecting liver injury, but was not impacted by associated muscle injury, which can increase circulating ALT levels. The findings were recently reported in *Toxicological Sciences*, including study results confirming the reference ranges of GLDH in a healthy human population, and the sensitivity and specificity of GLDH for detection of liver injury in humans. Jiri Aubrecht, Pharm.D., Ph.D., adjunct professor at Georgetown University and first author on the paper, said "biomarker development takes time and dedication of scientists across industry and academia. In fact, it has been more than 10 years since we published our initial GLDH study. Kudos to C-Path's Predictive Safety Testing Consortium for providing the environment and support for biomarker development."

The recently published paper included results showing that injury to tissues that are known to express appreciable levels of GLDH does not affect serum GLDH measurements, indicating serum GLDH is specific to liver injury and not to other tissue injury. The group also observed faster elimination of GLDH than ALT in humans, indicating that decreasing levels of GLDH could be considered a sign of a stop to additional liver injury. Most importantly, the study provided evidence of clinical sensitivity and specificity of GLDH for diagnosis of liver injury, along with current biomarkers of liver injury.

The U.S. Food and Drug Administration's (FDA) Biomarker Qualification Program (BQP) is currently reviewing C-Path's Full Qualification Package (FQP) to qualify GLDH as a liver safety biomarker. The long-term goal is that GLDH will be used more broadly to monitor liver health during drug development in clinical trials.

"Currently, the FDA and pharmaceutical companies rely heavily on ALT to detect liver injury during clinical trials," says manuscript co-author Mitch McGill, "but ALT has a few weaknesses, including a lack of specificity for the liver. Qualifying GLDH will be the first big step to address those problems."

Aubrecht is a Vice President, Head of Clinical Biomarkers at Prothena Corporation and Adjunct Professor at Georgetown University.

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About Critical Path Institute

Founded in 2005, as a public-private partnership in response to the FDA's Critical Path Initiative, Critical Path Institute® (C-Path) celebrates its 20th anniversary as a vital, independent, nonprofit. **C-Path's mission is to lead collaborations that advance better treatments for people worldwide**. Globally recognized as a pioneer in accelerating drug development, C-Path has established numerous international consortia, programs and initiatives that currently include more than 1,600 scientists and representatives from government and regulatory agencies, academia, patient organizations, disease foundations and pharmaceutical and biotech companies. With dedicated team members located throughout the world, C-Path's global headquarters is located in Tucson, Arizona and C-Path's Europe subsidiary is headquartered in Amsterdam, Netherlands. For more information, visit c-path.org.

Critical Path Institute is supported by the Food and Drug Administration (FDA) of the Department of Health and Human Services (HHS) and is 56% funded by the FDA/HHS, totaling $23,740,424, and 44% funded by non-government source(s), totaling $18,881,611. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, FDA/HHS or the U.S. Government.

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