publicly accessible CRC metabolome database to share this valuable resource: https://colorectal-cancer-metabolome.com/yale-university. DISCUSSION/SIGNIFICANCE OF IMPACT: This study provides the first CRC metabolome map, revealing metabolic differences across colorectal subsites. It challenges the right vs. left CRC classification, highlighting subsite-specific biomarker identification. Findings offer insights for personalized treatments tailored to the tumor type to improve patient outcomes.

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### The association between cell-free DNA and lung transplant survival

Rohan Meda[1], Yi-Ping Fu[2], Hyesik Kong[2], Moon Kyoo Jang[2], Temesgen Andargie[2], Woojin Park[2], Jae Lee[2], Ilker Tunc[2], Gerald J Berry[3], Charles C Marboe[4], Pali D Shah[5], Steven D Nathan[6], Michael B Keller[2] and Sean Agbor-Enoh[7]
[1]Georgetown University School of Medicine; [2]National Heart, Lung, and Blood Institute-NHLBI; [3]Stanford University School of Medicine; [4]New York Presbyterian University Hospital of Cornell and Columbia; [5]The Johns Hopkins School of Medicine; [6]Inova Fairfax Hospital and [7]Senior Author/PI, NHLBI

OBJECTIVES/GOALS: Lung transplant is a life-saving surgery for patients with advanced lung diseases yet long-term survival remains poor. The clinical features and lung injury patterns of lung transplant recipients who die early versus those who survive longer term remain undefined. Here, we use cell-free DNA and rejection parameters to help elucidate this further. METHODS/STUDY POPULATION: Lung transplant candidacy prioritizes patients who have a high mortality risk within 2 years and will likely survive beyond 5 years. We stratified patients who died within 2 years of transplant as early death (n = 50) and those who survived past 5 years as long-term survivors (n = 53). Lung transplant recipients had serial blood collected as part of two prospective cohort studies. Cell-free DNA (cfDNA) was quantified using relative (% donor-derived cfDNA {%ddcfDNA}) and absolute (nuclear-derived {n-cfDNA}, mitochondrial-derived {mt-cfDNA}) measurements. As part of routine posttransplant clinical care, all patients underwent pulmonary function testing (PFT), surveillance bronchoscopy with bronchoalveolar lavage (BAL), transbronchial biopsy (TBBx), and donor-specific antibody testing (DSA). RESULTS/ANTICIPATED RESULTS: Over the first 2 years after transplant, the number of episodes of antibody-mediated rejection (p) DISCUSSION/SIGNIFICANCE OF IMPACT: Clinically, early-death patients perform worse on routine surveillance PFTs and experience a worse degree of CLAD. These patients also have higher levels of cfDNA as quantified by n-cfDNA and mt-cfDNA. These results provide preliminary evidence that early-death patients have worse allograft rejection, dysfunction, and molecular injury.

## Regulatory Science

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### System theoretic process analysis: Identifying risks of the regulatory reliance ecosystem

Fatimah Noorii Sokeechand, Apurva Uniyal and Larry Liberti
University of Southern California

OBJECTIVES/GOALS: Identify risks in the regulatory reliance ecosystem, specifically for generic reliance pathways, using system theoretic process analysis (STPA), a proactive hazard analysis method, and create sustainable solutions to ensure global accessibility to the highest attainable standard of health. METHODS/STUDY POPULATION: A systematic literature review will assess the regulatory reliance ecosystem and interactions among National Regulatory Agencies (NRAs). This will involve using a hierarchical control structure (HCS) to identify operational loop failures, decision-making, and information flow. The HCS will inform an STPA to prevent adverse outcomes like patient harm or regulatory non-compliance. With IRB approval, 10 regulatory experts will also be interviewed to gather insights on risk scenarios. Their input will be used to integrate regulatory pathways into the HCS for adaptability, and a second round of interviews will be conducted to validate the scenarios and assess the effectiveness of recommendations. RESULTS/ANTICIPATED RESULTS: A preliminary literature review on regulatory reliance pathways from PubMed, WHO guidelines, and the DIA global forum, revealed potential risks in NRA interactions, such as overly redacted reports obscuring critical details and discrepancies in product versions or incomplete reviews affecting evaluations. Diverging guidelines and failure to adapt to country-specific needs are potential risks that also impact patient access to essential medicines. The STPA framework, along with expert feedback, will uncover unknown risks like "secondary-reliance" and soft risks, leading to sustainable recommendations to improve and optimize the safety of regulatory reliance. DISCUSSION/SIGNIFICANCE OF IMPACT: Safe regulatory reliance is crucial for global health equity and patient access to essential and innovative medicines. STPA will identify and address different layers of risk in the system, improving safety, efficiency, and innovation for timely patient access to therapeutics.

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### Evaluating global cosmetic regulatory frameworks using an adapted regulatory maturity benchmarking tool

Benjamin Ertl and Eunjoo Pacifici
University of Southern California

OBJECTIVES/GOALS: This research aims to modify an existing regulatory benchmarking framework, initially designed for medical products, to assess cosmetic product regulations in different countries. This tool will provide qualitative and quantitative comparisons of global regulatory approaches to cosmetics. METHODS/STUDY POPULATION: The World Health Organization's global benchmarking tool (GBT) was selected as a suitable template for the adapted methodology. The GBT contains a comprehensive set of functions, indicators, and sub-indicators defining the high regulatory maturity standard. Although the 269 sub-indicators are tailored to the regulation of medical products, they can be intentionally adapted for other products. Relevant indicators specific to cosmetic regulation will be identified to construct a customized benchmarking tool. This tool will then be used to assess the regulatory maturity of selected countries and regulatory authorities, including the United States, the European Union, Japan, India, Brazil, China, Ethiopia, and Nigeria. RESULTS/ANTICIPATED RESULTS: Preliminary analysis indicates a lack of harmonized standards for regulatory maturity across the global cosmetic market. The recent passage of the Modernization of Cosmetics Regulation Act of 2022 (MoCRA) has strengthened the United States' regulatory framework, incorporating 11 of 13 adapted maturity indicators. The United States joins the European Union (10/13 indicators) and Japan (8/13 indicators) as leaders in cosmetic safety and manufacturing transparency. Common basic policies included good manufacturing practice

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