A robust open science data platform for mechanistic disease discovery

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ABSTRACT

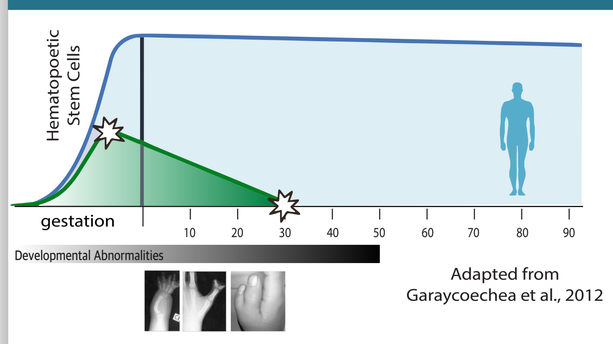
NEED: To address urgent unmet medical needs for rare diseases, coordinated mining of data sets are needed to find relationships between molecular and cellular processes and illuminate potential drug targets. Unfortunately, data sources are often dispersed, incompatible, and not useful for inexpert users.

GOAL: Develop a new biomedical "data Translator" for the rare disease research community that integrates multiple types of existing data across the translational spectrum, including objective signs and symptoms of disease, drug effects and intervening types of biological data relevant to understanding pathophysiology to develop new mechanistic nosologies.

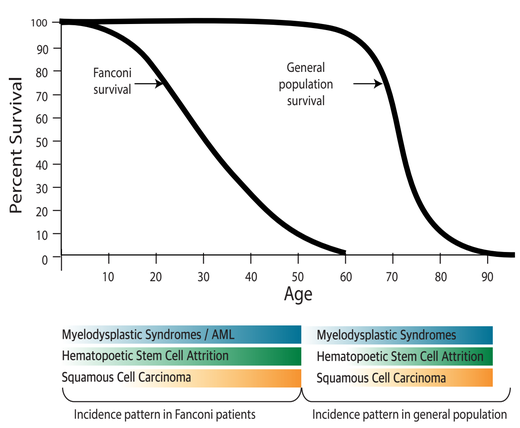
METHOD: Demonstrators will be used as pilots for initial development and evaluation of the Translator, (1) Diagnosis of patients with "undiagnosed diseases," patients for whom extensive evaluation by existing approaches has failed to identify an etiology for their symptoms. (2) Analysis of Fanconi anemia, a rare inherited multigene disease complex including gene-environment interactions.

EXPECTED OUTCOMES: We expect Translator will enable a robust rare disease research data ecosystem for granular mechanistic classification of diseases, improved diagnostics, prognosis, and treatment selection, and to support research by patients and advocates, basic scientists, drug developers, and clinical researchers.

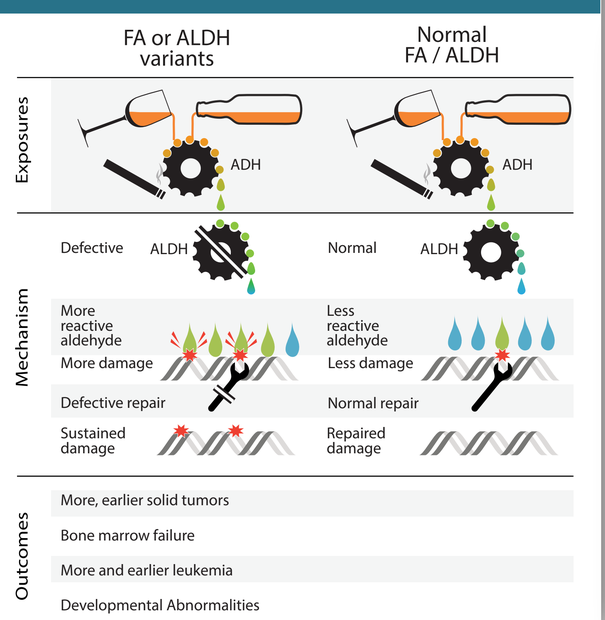
FANCONI PHENOTYPES



Adapted from Garaycoechea et al., 2012



FANCONI MECHANISM



FANCONI ANEMIA: COMPLEX ETIOLOGY

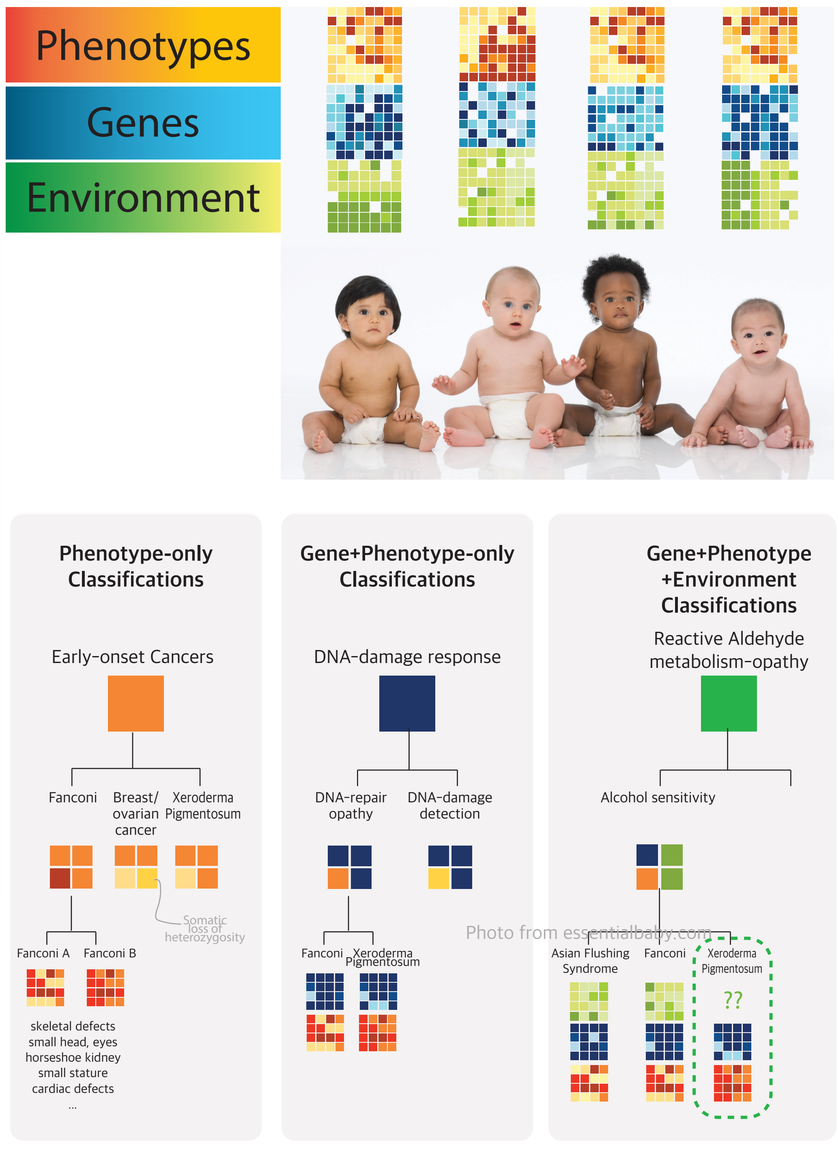
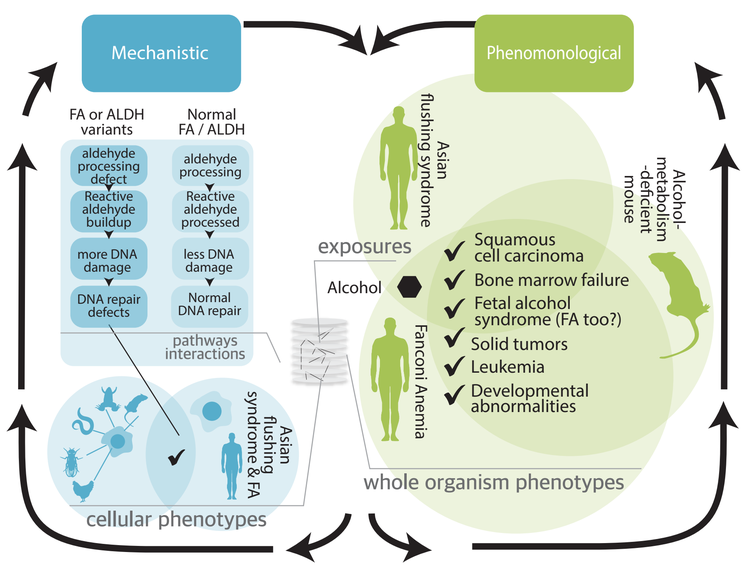
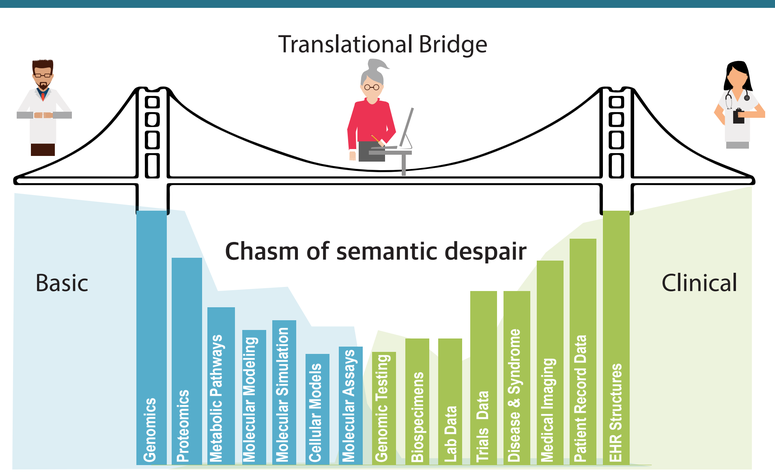


Photo from essentialbaby.com

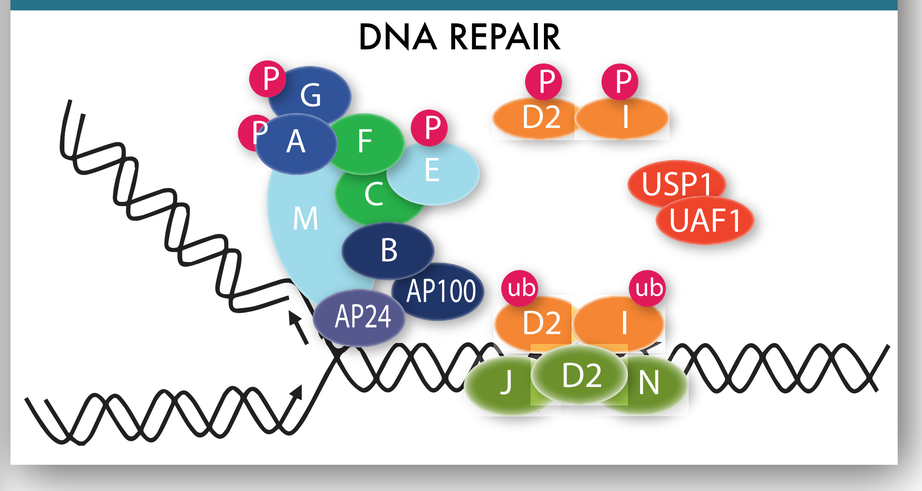
MECHANISTIC AND PHENOMONOLOGICAL BASIS



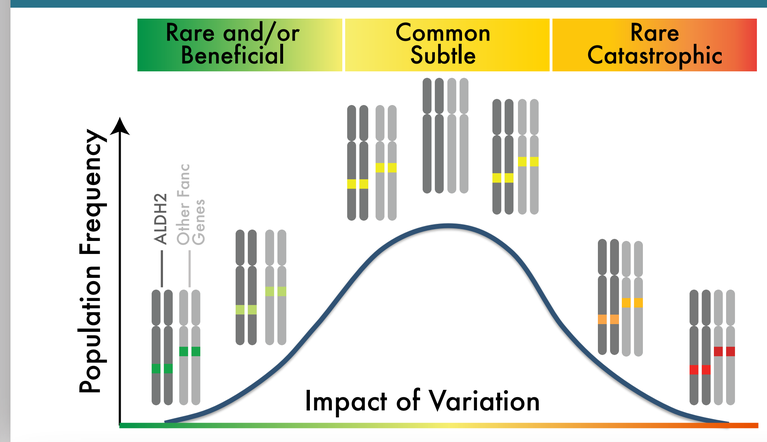
BRIDGING THE CHASM OF SEMANTIC DESPAIR



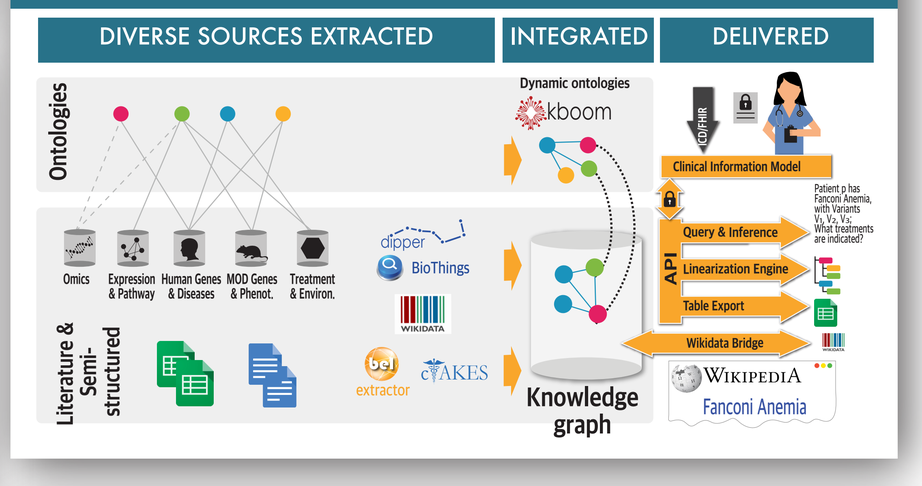
FANCONI PATHWAY



IMPACT OF VARATION IN FANCONI GENES



PROJECT APPROACH



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