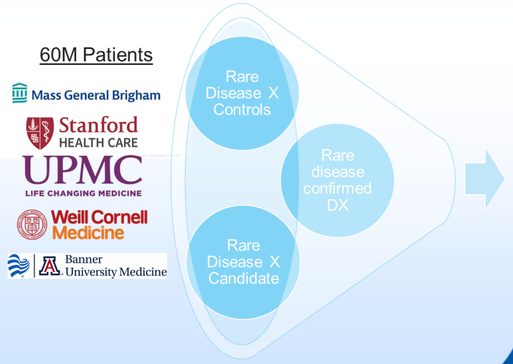
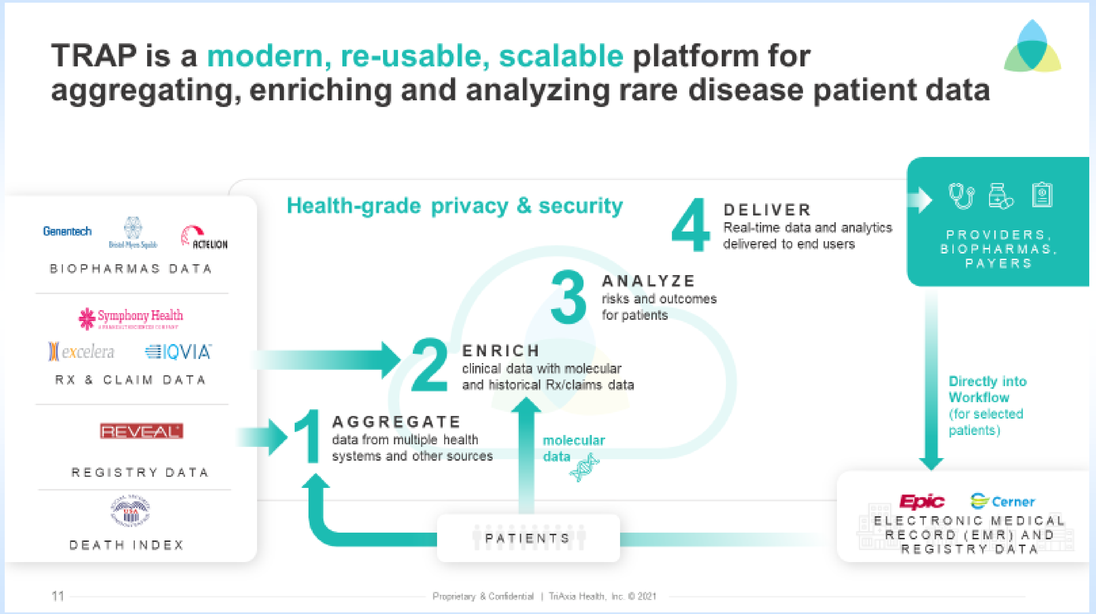
Application of clinical and molecular phenotyping to Pulmonary Hypertension using the TriAxia Health Platform

Rationale

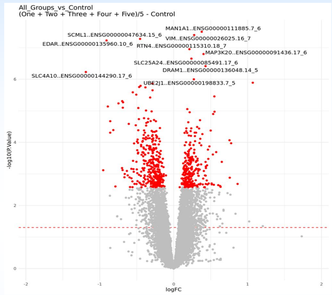
TriAxia Health, an Illumina Accelerator Company working with five academic pulmonary vascular disease programs, built a pilot version of their platform in Pulmonary Hypertension





Conclusions

Advanced glycation end products (AGE) and its receptor (RAGE) are involved in the pathogenesis of PAH



RAGE is a consistent marker in PAH and PH associated with lung disease.

Since RAGE causes BMPR2 and PPARγ downregulation, promoting PAH-PASMC proliferation, we speculate that the MAN1A1 gene is involved in the pathophysiology of groups 1 and 3.

Methods, Results & Authors

Enrollees underwent deep phenotyping including history and physical examination, cardiac and chest imaging, pulmonary function and six-minute walk testing, or exercise testing with gas exchange, and right heart catheterization. All blood samples were obtained at the time of right heart catheterization. RNA was bulk-sequenced and analyzed using limma with duplicate correlation. Genes with adjusted p-value <0.05 were considered significant

Leveraging the TriAxia Rare-disease Analytics Platform (TRAP), enrollees longitudinal clinical data, DNA (whole exome) and RNA were combined for analysis

To date, 650 patients have been enrolled, and 553 patients with PH had longitudinal clinical data, DNA (Whole Exome) and RNA processed. Differential expression contrasts of all five PH groups against healthy controls generated 5 down-regulated and 9 up-regulated genes (Figure 1). Of these, MAN1A1, involved in glycosylation, is up-regulated in PH compared to healthy controls (logFC of 0.37, adj.p<0.01). Most notably, MAN1A1 is shown up-regulated when separately comparing group-1 PAH (pulmonary arterial hypertension) and group-3 PH (due to lung disease) to healthy controls (logFC=0.36, adj.p<0.01 and logFC=0.39, adj.p<0.05, respectively).

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