Grand Challenge: Mapping Molecular Patterns- a blueprint to connect environmental, behavioral and socioeconomic stress factors to human disease and therapy

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Human genome project, a multidisciplinary collaborative program, has generated a map of all the genes for major sections of human chromosomes. In February 2001, Francis Collins, the director of NHGRI, noted that "the genome could be thought of in terms of a book with multiple uses: "It's a history book - a narrative of the journey of our species through time. It's a shop manual, with an incredibly detailed blueprint for building every human cell". But there isn't an encyclopedia for gene changes/reactions in response to various stressors like environmental (pollution/toxicants), behavioral, nutritional, emotional, psychological, socioeconomic or diseases like neurodegenerative, cardiovascular and prion diseases, cancer, atherosclerosis, diabetes, etc. Whether stressors "trigger" events or stressors "cause" the events still puzzle scientists around the globe. The whole human body reacts like a well-engineered giant biosensor. Almost all viable cell types in the human body release nanovesicles (50–100 nm in diameter, also known as exosomes). Exosomes contain biologically active molecules like proteins, RNAs, cholesterol etc (Figure A).

The molecular content of exosomes is a fingerprint of the releasing cell type and of its health status. The releasing cell communicates with other cells (either in the same tissue or in a distant organ) through these exosomes and influence the function of the receiving cell/organ (like a wireless communication). Therefore, the health of human body could be assessed through understanding these fingerprints. Interestingly, the molecular contents of the exosomes that are secreted in easily accessible body fluids (such as blood and urine) have proven to be highly specific, they represent a precious biomedical tool.

In particular, exosomes are valuable sources for biomarkers due to selective cargo loading and resemblance to their parental cells. Stem cells have been shown to mediate their therapeutic effects

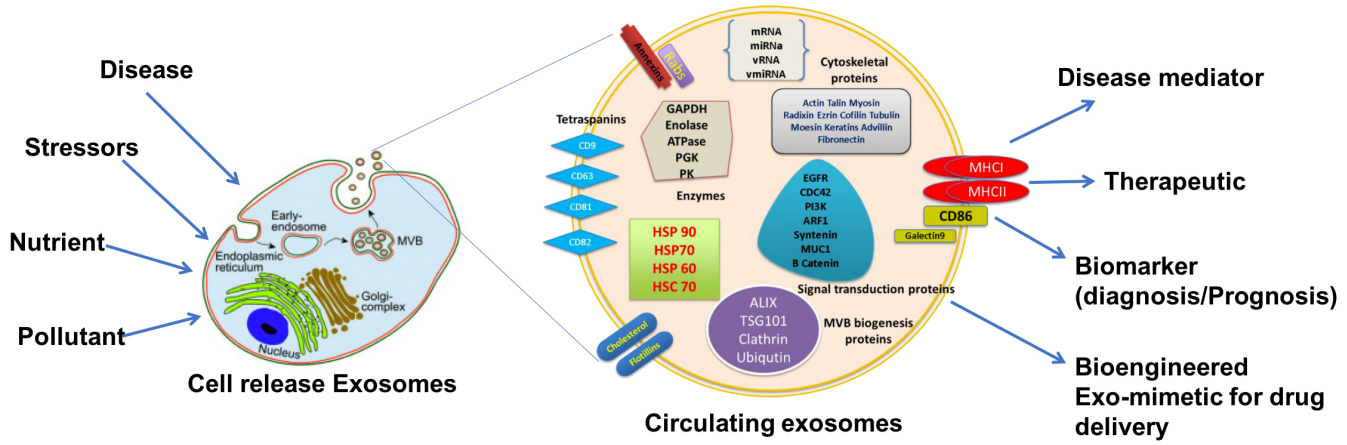

Figure A. Stress factors influence exosome molecular profile.
Pictures adapted from Progress in Lipid Research 2017, 66, 30-41 and Viruses 2015, 7(6):3204-25.

through secretion of these tiny cargo. Exosomes have a role in the spread of some types of viruses such as Epstein-Barr virus and rotavirus.

Mapping Molecular Patterns program

Identifying and mapping these molecular fingerprints in human population subjected to diverse stressors in different geographical locations would generate the next generation of valuable scientific tool for future game-changing applications.

Some of the applications:

- Precision medicine: Exosomes contain disease biomarkers or carry potential therapeutic molecules, thus representing the ideal nanotheranostic approach, with a very high potential in the field of personalized medicine.
- Health care: The tool equips health care providers with immense insights to understand, diagnose, prevent and/or cure disease. Stem cell-derived exosome or bioengineered exosome mimetics, in combination with a delivery vehicle, could be used in regenerative medicine.
- Endogenous Biosensors- The molecular finger prints could reveal patterns, trends, and associations, especially relating to human behavior and interactions with environment.
- Broader applications, monitoring & policy making: The molecular profiles could play an instrumental role in predicting disease, socioeconomic stress patterns (like long commute, psychological, drug overdose epidemic, prison environment, pollution, infections etc) or even predict environmental clean-up efforts. Creating healthier community requires quantitative assessment of the benefits achieved. Certain molecular patterns might evaluate the benefits and might aid in policy making.

The UAB *Mapping Molecular Patterns* program will comprise of leading scientists, working together, from multiple disciplines like precision medicine, big data, health care, proteomics, genomics, bioinformatics, tissue engineering, social workers, educators, stem cell biologist etc. The program will place UAB at the forefront of research innovations and community service and allow convergence of varied disciplines to map molecular patterns that could link stress factors to health/disease patterns. The program will accelerate research innovation at UAB, develop technological platform for disease diagnosis, therapeutics, biomarker and attract partnership with UAB faculty, students, health industry and external players.

Potential collaborating teams:

Biomedical Engineering, Biostatistics, Material Science
Medicine, Precision Medicine
Transport, Psychology
Genomics, Proteomics
Computational analysis
Veteran Affairs hospital (UAB campus)