

Streets of Philadelphia¹

(Comments from the 2013 Annual ATS Conference)

In many medical conferences and meetings we can find hordes of redundant research that little adds to the current knowledge and practices, with the impression just like chewing the same things over and over. This was not the case of the American Thoracic Society (ATS) 2013 Annual Conference that was held in Philadelphia, also called "the city of brotherly love". The Convention Center is just located in the Old City, as to say "the richest square mile in the history of America", but for me it was mostly important to participate into the scientific meeting with both curiosity and intensity at my best. The ATS conference is a comprehensive scientific event where anyone can find anything and everything: from the discussion of clinical cases, to the state of the art on exacerbations of COPD, or a course on the diseases of the pleura. But alongside these "usual" clinical topics there is really wide and diversified offer of what is emerging in the field of respiratory basic science and translational medicine. The majority of the sessions are in fact classified as "Basic-Clinical-translational" or "Clinical translational," or only "Basic" or "Translational". I am fully convinced that dividing science from clinical medicine is only negative for the patients, but the organizers of the ATS meeting think the same, I supposed. At Philly, I followed the whole session on cell biomechanics to be aware on how the cytoskeleton-matrix interactions guide the behavior of cells, in particular those progenitor, and also the methods to study lung injury and its repair. Molecular interactions between the cytoskeleton and extracellular matrix govern a wide range of cellular behaviors in lung pathological conditions of great clinical impact like pulmonary fibrosis, chronic obstructive pulmonary disease (COPD), asthma, ARDS, and severe sepsis. Understanding how cell biomechanics contribute to various respiratory diseases can help to find new pharmacological strategies. Another very interesting topic was regenerative and reparative medicine. Airways and pulmonary regeneration/repair were studied in mice (much less in humans). Cell proliferation is evaluated in the mouse entering a label (tag) gene within the cell and following the trace genetic (lineage tracing) in proliferating cells and differentiating. Clones of genetically marked cells are then identified experimentally in differentiated cells within the tissue, maintaining the genetic characteristics of multipotent progenitor cells. Also in humans the resident stem cells or progenitor cells are present and active, albeit with low intensity for most of human life, but there is no clear evidence of cell lineage as in the mouse because of obvious ethical problems to insert a marker gene in patients. After any injury the progenitor cells first change their shape and their consistency prior to differentiate and proliferate in response to an external trauma. The correct tissue regeneration usually leads to a repair of the damage with functional recovery. Nevertheless, sometimes we can have reparative aberrations that lead to progressive diseases, as in the case of idiopathic pulmonary fibrosis and pulmonary emphysema-COPD. Not surprisingly, the senescence of tissue stem cells may have an important pathogenic role in both pulmonary fibrosis and emphysema. In fact, idiopathic pulmonary fibrosis and COPD are typically diseases that affect people of middle age or older, with pathological characteristics showing typical aspects of cellular senescence such as telomere dysfunction. Going to see inside the cell with nanotechnology means such as atomic force microscopy (AFM) we can study the cell stiffness in various pathological situation, but you can also identify the badly-assembled proteins (misfolded) that "engulfing" the endoplasmic reticulum will cause stress that leads to apoptosis and then to cell death. All these data soon will lead to the reconstruction of the pathological puzzle of various untreatable diseases like pulmonary fibrosis, and ARDS, and new treatment modalities in the next future will take advantage of lung's ability to regenerate itself. Another important recent field of translational research is the application of "omics" in the clinical setting. New data about metabolomics of severely ill patients were presented at Philadelphia by a Brigham and Women's Hospital/Harvard Medical School's research team. The metabolic profiles of severely sick patients could be used to predict patient risk of death in the intensive care unit (ICU).

¹ Bruce Springsteen won a Grammy and an Oscar for this song, the theme from *Philadelphia*, which starred Tom Hanks in his first Academy Award.

A prospective study, involving 90 ICUs and two populations of patients with systemic inflammatory response syndrome, sepsis, or sepsis/acute respiratory distress syndrome, showed that those dying before day 28 differentially expressed metabolites, compared with survivors. Then, using statistics to create a predictive model, the researchers identified a network including four metabolites – sucrose, methionine, beta-hydroxyisovalerate amino acids, and mannose from the carbohydrate pathway and arginine – that were closely associated with mortality in both populations studied, so they can be used as a tool for identifying patients at highest risk for death in the ICU. Finally, the 2013 ATS meeting encouraged any attempt to carry life sciences to the patient's bedside, and it is what we really need today. Nevertheless, I'm also aware that several colleagues of mine do not agree this attitude, but they prefer still think to medicine as an art. However, if anyone thought that the daily clinical practice is simpler than life sciences, probably he/she does not ask the right questions. On the other hand, if anyone thought life sciences is too complicated for clinicians, probably he/she does not put enough right questions too.

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