

Mineral dust induced pneumoconiosis: a pivotal role for the inflammasome

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By definition, pneumoconiosis refers to a group of diseases that are caused by the inhalation of organic and inorganic dusts that remain in the lung. It is one of the most important occupational lung diseases especially in under developed countries. Many fibrotic diseases nowadays are furthermore becoming leading causes of morbidity and mortality in the aging population of western society. Each year circa 450.000 persons die because of the consequences of pneumoconiosis. Although disease incidence has declined in developed countries, it is still prevalent and especially of health concern in many poorly surveyed countries with less compliance towards regulatory standards as well as protective and preventative measures of exposure to workers. The actual total figure of prevalence and incidence of death might be much higher since under-diagnosis and under-reporting are quite common. No curative treatment exists currently against silicosis, stressing the urgency of the problem. While significant progress has been made in our understanding of the biology of inflammation, fibrosis and aging in recent years, their interrelations remain largely speculative. Further investigation of the real etiopathology of the disease is therefore still very important. In this thesis, it is reported that crystalline particles and fibers activate an important multiprotein named the inflammasome (and possibly also other subtypes) which is involved in the progress of the disease symptoms and its development. The observation that it was possible to extrapolate in vitro and animal work data of visualized inflammasome activation into the clinical patients with pneumoconiosis has, in addition to its scientific evidence, a huge social relevance for many reasons.

In addition to the academic community, these research results can be important for a multitude of persons with a broad spectrum of varying interests. First of all, miners or others that are occupationally or accidentally exposed, but also their family members or civilians with much interest in medical facts or environmental research can benefit from the important new information. Dissemination of awareness about the irreversibility of the disease will lead to better preventive strategies for miners as well as mining companies to reduce the risk of exposure. Occupationally exposed workers will be more informed than before and everywhere it can be expected to have better compliance to reduce risk standardized protocols. This has a big impact on general safety and will lead to improved patient management. Unfortunately, a paradigm shift with respect to worldwide preventive approaches is still mandatory.

The results could immediately lead to adapting standard operating protocols by including immunological staining in biopsy material from persons with a high risk factor for disease development patients. Implementing additional methodology to enrich diagnostic medical imaging procedures to screen for disease pathology in humans will be innovative. As a result and for obvious reasons insurance companies that are occupied with single or familial autopsy cases will also benefit from the exposure to these research results. With no huge risks involved, new standard operating procedures for workers either or not related to occupational medicine can be implemented consisting of biomarker measurements in lavage fluid of

patients or by staining resection material, all in parallel with existing medical imaging procedures.

With indications of new avenues in silicosis diagnostics supporting ongoing medical imaging it is clear that research and development departments of pharmaceutical companies will be very interested to start and evaluate the processing of new diagnostic kits that will facilitate early diagnosis of the disease. In the field of biopharmaceutical developments, early detection via the development of disease with diagnostic kits could improve quality of life of hundreds of thousands of workers annually worldwide. Moreover, there could be an impact economically as further substantiated results will lead to attract funding, spin-off collaborations and the creation of more jobs. With respect to pharmaceutical diagnostic tools, product research & development and public relations as well as media we see largely enhanced market opportunities. With optimized communication tools and collaborators in taskforces the cost can remain very low. Development of innovative kits by spin-off or pharmaceutical companies will be very costly depending on size of production and types of specific antibodies, however the return of investment is gigantic and societal impact on job creation could also be improved. Aside from the existing product developing companies, it could also be interesting for startup entrepreneurs that have the idea to think globally on mask fabricating industry in line with offering optimized tools to people that may help decrease the risk of exposure to harmful particulates. Lastly, animals and animal activists profit since the findings will help to refine, reduce and replace the animal experiments in the future. All together, these results will have a not negligible societal impact.