

## Biosignatures distinguish between tuberculosis and sarcoidosis

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With a range of diseases, doctors need unique features which they can use to unequivocally identify a patient's illness for an appropriate diagnosis. Scientists therefore search for the biomarkers for an illness or a combination of biomarkers, known as biosignatures, which are as easy as possible to measure. Researchers at the Max Planck Institute for Infection Biology in Berlin have now created complete gene and microRNA expression profiles together with important inflammatory mediators in the blood of tuberculosis and sarcoidosis patients. Although they have identified a signature that distinguishes healthy individuals from patients, the biosignatures of both diseases are nevertheless very similar. It is almost impossible, therefore, to distinguish between tuberculosis and sarcoidosis with just a single signature. A set of different biosignatures is better suited for distinguishing in a first step between diseased and healthy individuals and, in a further step, between the specific diseases.

Biosignatures cover a profile of different features, which can be used to identify diseases and distinguish them from similar clinical pictures. These features include the presence of mediators and gene expression profiles in the blood. In recent years, for example, researchers have discovered signatures for tuberculosis, which doctors can use to distinguish between patients with tuberculosis and healthy individuals.

Equally important is the distinction between different diseases with similar clinical appearance, such as tuberculosis and <u>sarcoidosis</u>. Therefore, using gene and microRNA expression in <u>blood cells</u> and



inflammatory mediators in serum, the scientists at the Max Planck Institute for Infection Biology selected sets of markers characteristic for tuberculosis and sarcoidosis patients. Although both diseases primarily damage the lungs and produce similar symptoms, they have very different causes. While tuberculosis is caused by an infection with bacteria, sarcoidosis is not contagious.

Studies show that the two diseases are not only similar clinically; their biosignatures also have a number of elements in common. Compared to healthy individuals, most genes in sarcoidosis and tuberculosis patients are regulated in a similar way: "Of approximately 13,000 genes whose expression differs, depending on whether the individual is healthy or diseased, approximately 9,000 genes are expressed in the same way in both diseases. Only 700 genes differ in their expression between tuberculosis and sarcoidosis patients – but these can be used to unequivocally identify the two diseases," says Stefan Kaufmann from the Max Planck Institute for Infection Biology.

In addition, microRNAs, which modulate the formation of certain proteins by inhibiting gene expression, appear in a similar pattern in both diseases. In total, around 150 microRNAs shared by both diseases differed from healthy individuals. Only four microRNAs are suitable for distinguishing tuberculosis and sarcoidosis patients. The overlap is less pronounced in the profile of inflammatory substances in the blood: while only one of these cytokines is modified equally in tuberculosis and sarcoidosis compared to healthy individuals, twelve of these signal mediators are suitable for distinguishing between the two diseases.

The results obtained by the Berlin researchers show that modified biomarkers can be traced back to processes that occur not only in one specific disease, e.g. immune responses. The immune response therefore draws on the same basic elements in different clinical pictures, and only a few of these elements are specific to a particular disease. These



commonalities also reveal a lot to scientists about the general causes and mechanisms underlying many diseases.

A single biosignature is therefore not enough to distinguish between healthy and diseased individuals, and to distinguish between different diseases with a similar clinical phenotype. Although the combination of many genes increases specificity and sensitivity in distinguishing between healthy and diseased individuals, it automatically leads to a lower specificity compared to other clinical pictures. "Instead, we should first of all distinguish between healthy and diseased individuals and then separate the individual diseases from one another in the next steps. We can then unequivocally identify a <u>disease</u> using a handful of genes per step," explains Kaufmann.

This means that doctors could concentrate on diseases that actually occur locally. In African countries, where tuberculosis is widespread, it would then be possible to identify <u>tuberculosis</u>, AIDS and malaria quickly.

**More information:** Common patterns and disease-related signatures in tuberculosis and sarcoidosis. Jeroen Maertzdorf, January Weiner, Hans-Joachim Mollenkopf, TBornotTB Network, Torsten Bauer, Antje Prasse, Joachim Müller-Quernheim and Stefan H. E. Kaufmann, *PNAS*, May 2, 2012. <a href="https://www.pnas.org/cgi/doi/10.1073/pnas.1121072109">www.pnas.org/cgi/doi/10.1073/pnas.1121072109</a>

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