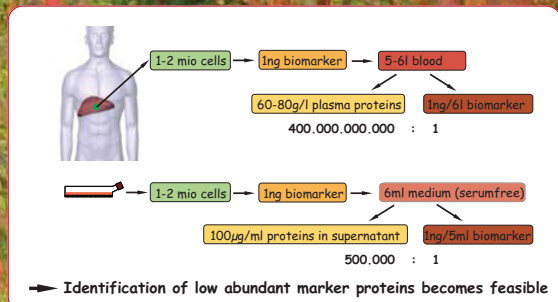
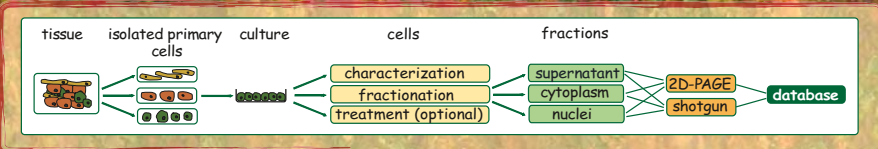


Systematic biomarker discovery by secretome analyses of disease-associated primary human cells.

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To give an example, normal lung fibroblasts from healthy background (HLF, Pool A) were compared to fibroblasts isolated from lung adenocarcinoma tissue (Figure 1)



Figure 1

57 proteins were found secreted at increased levels when comparing the tumor-associated cells with the fibroblasts derived from normal background. Amongst them we identified proteins with lower expression specificity such as Collagen alpha-1(I) (Fig. 2), and proteins with higher expression specificity such as bone morphogenetic protein 1 (Fig. 3).

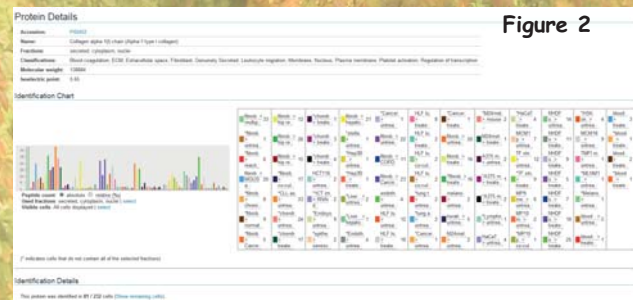


Figure 2

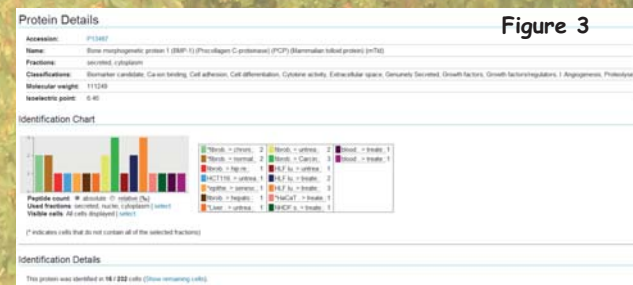
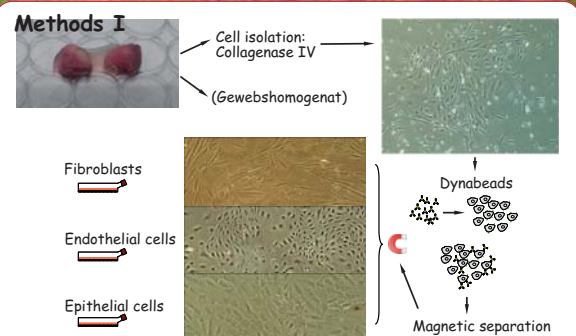


Figure 3



Conclusion:

We have built a database currently comprising 10.668 different proteins out of 2.626.000 peptide identifications identified from the analysis of 232 different cell types/cell states (Fig. 6). As all cells were analysed using the same standard operation procedure, the database gives a unique overview of protein expression with respect to the cell type specificity and relation to functional activation.



Figure 6

Motivation

Characteristic functional cell alterations are consequent to any disease

Proteome alterations occur consequent to any functional cell alteration

Therefore, all diseases are accompanied by characteristic proteome alterations

Biomarker do exist but may hard to find

The subcellular distribution of proteins according to GO terms was highly similar (Fig. 4).



Figure 4

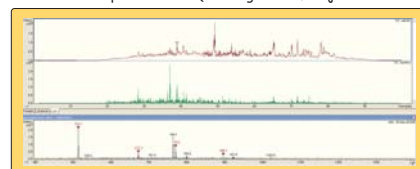
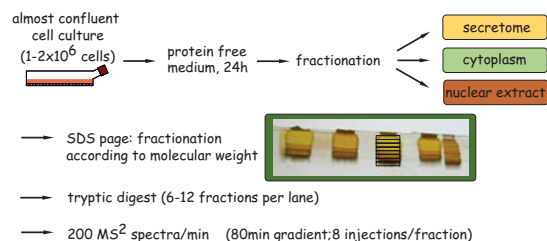
Some of the identified proteins showed a clear relation to functional activation such as PTX3, which was found induced upon inflammatory activation of normal fibroblasts with Interleukin-1beta (Fig. 5: Thy-1/CD90 is a marker for fibroblasts). We use such marker proteins for functional classification of cells.

Figure 5



The database allows us to find proteins specifically expressed in tumor-associated stroma cells. The identification of mechanisms causing the expression of these proteins supports the design of targeted therapies for the suppression of stroma-derived tumor promotion.

Methods II



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