CliNETx Scientific Information Summary

We aim to advance our existing systems for structured clinical data entry for the health history and physical findings and the scan solution with generation for optical character recognition based and primary electronic patient documentation. We suggest to use patterns and content of structured data entry as a basis for structuring unstructured content in the electronic documents for analysis in research and clinical routine care. The incorporation of all routine laboratory results in a database for computational analysis forms a critical part of our proposal. Within the routine laboratory imaging of leukocytes is captured and utilized for the differential counts of different types of these blood cells. In coordination with the basic experimental part of our submission, we will be attempting to identify and classify so far not classified cells mostly considered artifacts. Finally, we will address the crucial question of factors that underlie the increased propensity of polymorphonuclear granulocytes, a type of white blood cells, to extrude their nuclear chromosomal DNA in a process termed neutrophil extracellular trap generation.

The proposal is weighted toward the rather mundane, but nonetheless highly important field of clinical documentation, primarily in rheumatoid arthritis (RA), and by extension other rheumatologic conditions and their co-morbidities. As a complex, chronic disease with multiple co-morbidities arising during its course, RA is a highly suitable model disease for this purpose. There is also a whole range of tools to classify the diagnosis and to assess the activity and outcome of RA, which can be used as a basis for data structure. Integrated in the structured data entry is a report generator that creates a real-time report with semantic arrangement of text content. Apart from the savings in physician resources promised by the report generator, it is critical to provide the clinician with control over the content of data entry. To this end, the system development is directed toward a domain language that is independent from the underlying program and in its final form will allow the clinician, as the domain knowledge expert, to define his data entry content without the aid of a programmer. Regarding the content structuring and analysis of unstructured machine-readable paper and electronic documents, we have elaborated a concrete concept to achieve an automated, deep and broad information base for computerized analysis. This will make the data accessible for clinical and all purposes of research questions. With the data in an accessible format we expect that research at the patient level will be facilitated and more attractive for basic researchers.

To amplify the impact of structured clinical data, we have conceived the integration of all routine laboratory results into the analyzable dataset. This will allow the correlation of clinical findings and outcomes with laboratory parameters covering aspects of inflammation, kidney and liver function, among many others.

To complement the clinical aspects, we propose to apply the insights of neutrophil extracellular trap formation to clinical diagnostics utilizing the imaging of leukocytes captured for differential leukocyte counts. While this provides a translational aspect against which to test the clinical dataset, we envisage building on previous data from our group and others to further investigate the novel and promising findings on increased neutrophil extracellular trap formation in rheumatoid arthritis and the accompanying dysregulation of neutrophil granulocyte signal transduction. Because extracellular trap formation goes in hand with citrullination of histones and other targets, it very likely generates the antigens that are targeted by anti-citrullinated peptide antibodies in RA. Neutrophil involvement also suggests mechanisms by which environmental factors contribute to the pathogenesis of RA. As the next steps in investigating this issue, we plan to analyze the proteome, transcriptome and multiple cytokines related to neutrophil granulocyte function in RA. This will be studied in different stages and activities o the disease. These experiments will be all the more interesting in that they have yet to be reported in RA.

The initial encouragement for us to assemble and submit this proposal came from Director of SystemsX after a demonstration of the current versions of our automated document scan system with generation of electronic documents by optical character recognition, the searchable patient database and the applicability of the structured direct clinical data entry. The challenge was to embed a significant basic systems medicine project, which we have addressed by utilizing the structured clinical dataset for the clinical information needed.

The research and industry partners contributing to this proposal all have extensive expertise and track records in their fields. The institutional settings for the research are well matched for the envisaged project, and we trust that we can meet the expectations of the ambitious aims, both from the clinical point and in the relevance of the laboratory experiments.