

- Angiogenesis is driven not only by hypoxia, but also by proinflammatory mediators produced by immune and stromal cells
- Many pathways downstream of these proinflammatory stimuli contribute to various cellular processes involved in angiogenesis
- Targeting proangiogenic pathways to inhibit neovascularization has been successfully exploited in several cancers, and may also prove beneficial in the treatment of chronic inflammatory diseases

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#### SP0049 DNA AGGREGATES AS ALARMINs

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DNA is a large polymeric molecule that displays powerful immunological activities and operates in the context of multi-component aggregates to alarm the immune system and stimulate innate immunity. Although DNA has important roles in normal host defense, DNA can serve as an autoantigen and autoimmunogen by itself or in association with other immunologically active nuclear molecules. In the setting of systemic lupus erythematosus (SLE), DNA is a key target antigen; while antibodies to pure DNA double stranded DNA serve as important biomarkers, the relevant antigenic form of DNA during disease is the nucleosome in which DNA is bound to histones. Furthermore, nucleosomes can be components of microparticles which are small membrane-bound structures that are released from dead and dying cells. MPs can stimulate immune responses and serve as a nidus for immune complex formation. In normal immunity, DNA can interact with nucleic acid sensors in the cytoplasm of cells to stimulate responses including production of type 1 interferon. These sensors respond to DNA from intracellular organisms such as bacteria and viruses although damaged DNA and DNA from mitochondria can also interact with these receptors. While these sensors are intracellular, they can interact with extracellular DNA that is introduced or transfected into the cell; this translocation event occurs with DNA bound with other molecules. In another facet of host defense, DNA can be released from neutrophils during a process termed NETosis. A NET or neutrophil extracellular trap is a mesh-like structure comprised of DNA as well as granule proteins that have antibacterial activity. NETs can trap and kill bacteria. Thus, in its diverse immunological roles, DNA interacts with other molecules to form aggregates or sub-cellular structures that alarm the immune system, promote host defense or drive critical events in autoimmunity.

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### Bringing rheumatology research to the next level: addressing the main challenges of patient partnerships in research and health care service design

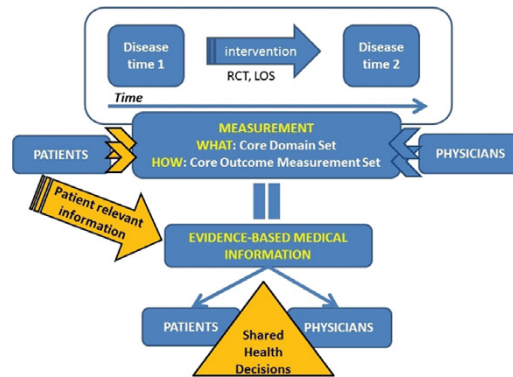
#### SP0050 ENSURING REPRESENTATIVENESS OF THE PATIENTS' PERSPECTIVES IN THE FINAL RESULTS GENERATED FROM CLINICAL RESEARCH – CHALLENGES FROM THE PERSPECTIVE OF RESEARCHERS

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Now more than ever, patients are increasingly taking part in shared healthcare decisions with their physicians. Information from clinical research, on which evidence-based medicine draws upon, ideally needs to make sense to patients and not only physicians.

*Representativeness of the patients' perspectives in the final results of clinical research is therefore critical for shaping the content and quality of medical knowledge and for shared clinical decision-making.* As a result there is increased emphasis and even requirement from organizations around the world to include patient research partners (PRPs) as equal members in the medical research team. PRP inclusion means participation in research question generation, study design, data analysis/interpretation, authorship and results dissemination. Several questions remain: 1) How can we maximize the impact of the perspective patients bring to the table? 2) How can we ensure we capture the patients' perspective accurately and carry it forward into the final product of research? We can maximize impact and reach by including the patients' perspective in research that defines the way we assess disease and disease targeted interventions. Randomized controlled trials (RCTs) and longitudinal observational studies (LOS) are currently our main source of clinical information regarding efficacy of disease targeted interventions. Outcomes assessed in RCTs and LOS, as well as the health measurement tools used to assess these outcomes need to include the patient perspective in order for the information generated from these studies to be valid and usable. A conceptual diagram to illustrate how the patients' perspective is

critical in generating health information for patient and physician shared decision making is represented in the Figure.



**Case study: the updated Psoriatic Arthritis (PsA) Core Domain Set patient domains.** A core domain set is the minimum set of outcomes that need to be assessed to evaluate the effect of disease targeted interventions. The first PsA core domain set was developed in 2006 by physicians and methodologists. The core set update study identified clinical trial outcomes important for patients as a group and for physicians as a group and reconciled both perspectives to recommend an updated PsA core domain set that represents the perspective of both patients and physicians. Five PRPs were members of the working group and contributed during all stages of the project. The perspective of patients was included as follows: a) domain generation through qualitative data collection and analysis from international focus groups; b) first domain prioritization exercise in electronic surveys with patients and physicians; c) a face to face nominal group technique meeting with 12 patients and 12 physicians to prioritize domains; d) second domain prioritization exercise through electronic surveys with patients and physicians; e) discussion and voting at the 2016 Outcome Measures in Rheumatology conference. During the process of achieving consensus we observed the following dynamic for patient prioritized domains (percentages represent proportions of patients ranking each domain important in the first survey and then the second survey): 1) Pain was rated important by 76% of patients in the first survey and 82% in the second survey and remained a core domain; 2) Fatigue 78% then 71% and became core domain; 3) Physical function 72% then 80% and remained a core domain; 4) Participation (daily activities and employment/work) was important to 72–76% of patients in the first survey and to 78% in the second survey and became a middle circle domain (important, not required); 5) Emotional well-being 60% then 57% and was placed in the middle circle; 6) Independence 82% then 63% and placed on the research agenda. In each of these situations the trend in the patient's vote as a group followed the physician's vote with one exception: the domain participation.

**Summary of challenges and solutions for ensuring representativeness of the patients' perspective in the final results:** Patients may change their views and align with physicians during the course of a research project. PRPs can help increase awareness of the patients' perspective throughout all stages of the research process. Special attention should be given to: 1) use of methods that adequately capture the patient perspective in the initial stages of a research project, and 2) allowing a robust patient perspective to take shape from patients as a group, before the consensus process with additional stakeholders begins. In addition, supporting patients with adequate information and materials and involving PRPs in their development will maximize understanding of the task for patients and their full participation.

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#### SP0051 BECOMING A PATIENT RESEARCH PARTNER IN THE FIELD OF RHEUMATOLOGY. MY EXPECTATIONS AND THE CHALLENGES OF BEING EDUCATED AND TAKEN SERIOUSLY

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Patients often feel that their experience of illness is not valued nor understood by others. However, there has been a growing recognition of the importance of the patient perspective and involvement in research, improving its methodology and outcomes. The European Medicines Agency has been involving patients' and consumers' representatives on their work since 2005. The "European League Against Rheumatism recommendations for the inclusion of patient representatives in scientific projects" have been published in the "Annals of the rheumatic diseases" in 2011.

I was diagnosed with Juvenile Idiopathic Arthritis when I was 5 years old, back in 1977. Therefore, I have 40 years of experience of living with a Rheumatic and Musculoskeletal Disease (RMD), but no recollection of what my life was like "before" and "after" the diagnosis. I have learned to live and cope with my RMD, with a sense of being different from my peers. This sense of "uniqueness" was