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Flow cytometry in the clinical laboratory

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This issue of the eJIFCC is dedicated to highlight some aspects of clinical flow cytometry. In the past 50 years several techniques have revolutionized laboratory medicine. Undoubtedly flow cytometry is one of those, with a substantial impact on diagnosing and monitoring diseases in laboratory hematology, hemostasis and immunology. The development in flow technology also exerted a considerable effect on the accuracy of testing, as well as on turnaround times and on the objectivity of the reported data. Although morphological investigation of peripheral blood and bone marrow smears has remained a gold-standard in diagnosing malignant hematological disorders, recently flow cytometric studies are an absolute requirement in finalizing the diagnosis of de novo leukemias, while in other areas, like minimal residual disease detection it completely replaced morphology and has become a technique that can reliably identify 1 leukemic cell in 10,000 normal cells. Platelet glycoprotein abnormalities, reticulated platelets, as well as activated platelets are all diagnosed today by flow cytometric techniques. For certain red blood cell disorders like paroxysmal nocturnal hemoglobinuria and hereditary spherocytosis, flow cytometry is a key technique. This method is required also in the diagnosis of immunodeficencies, autoimmune disorders, antigen specific T-cell responses, allergy-testing and is utilized in transplantation immunology.
The wide repertoire of these diagnostic applications was made possible partly by the large arsenal of probes – e.g. directly conjugated monoclonal antibodies, fluorescent probes for cell function and viability – as well as by the constant improvement of the flow cytometers. Today, CE labeled benchtop analysers are routinely equipped with
2-3 lasers and can provide 8-10 color labelings with a high event rate per second, thus enables the acquisition of 0.5-1 million cells in a reasonable time frame. Along with these developments in hardware and reagent supply, new softwares have been developed. Thus, cytometrists can analyse and provide interpretative report for a large number of clinical samples in a relatively short time, not mechanically reporting percent positivities for individual CD markers, but by describing only key phenotypic findings and corrrelating staining patterns to diseases.
Clinical research and laboratory diagnostics can not always be sharply separated in flow cytometry. What is regarded today as a research tool can soon turn to a diagnostic assay.

This issue of eJIFCC provides some examples for the versatility of this technology. The first paper describes the state of the art multicolor flow analysis of myelodysplasia. The second publication is on a functional assay to identify the multidrug resistant phenotype in hematological malignancies. Cardiovascular disorders like myocardial infarction and stroke are exemplified by the presence of activated platelets. The third article depicts the possibilities to identify activated platelets by flow cytometry. The fourth paper deals with a different approach, where we are analysing soluble plasma proteins by a flow technology that uses either beads or cells as a reagent. Finally the analysis of intracellular calcium as a cell signalling event as well as a potential disease marker is described by flow cytometric methods.
I am fascinated how, this ever-growing technology influenced our daily work in the past decades and I am sure that at least two different directions of future developments will prevail. Most likely many assays will be applied to smaller scale equipments, that will be affordable by more and more laboratories while on the other hand, frontline applied research will generate diagnostic tests in many areas of cell biology – apoptosis studies, phosphoprotein and cell cycle analysis - that today are carried out mostly only in research applications.