

Biomarkers and Endometriosis: The Need to Move Beyond Innovation to Validation

Preface

This book presents a state-of-the-art description on how much progress has been made in the development of a noninvasive test for the diagnosis of endometriosis.

Such a test is much needed, especially for the early detection of endometriosis of symptomatic women with pelvic pain and/or subfertility without evidence of endometriotic cysts, nodules, or adhesions on gynecological ultrasound. This would include nearly all cases with only peritoneal endometriosis, some cases of moderate–severe endometriosis without a clearly visible ovarian endometrioma, and cases with pelvic adhesions and/or other pelvic pathology undetectable by gynecological ultrasound. Ideally, this test could also substitute gynecological ultrasound and allow the diagnosis of endometriosis in areas where ultrasound is not available or reliable. The main aim of such a test would be not to miss any woman who might benefit from endometriosis surgery to improve pelvic pain and/or subfertility. In that context, a test is needed with high sensitivity (ideally more than 80%) and acceptable specificity, fully accepting the risk that a laparoscopy will be negative in some women [1]. This risk can be balanced by the advantage that a negative laparoscopy can assure women with pelvic pain and/or infertility that their pelvic anatomy is normal and allow other diagnostic/therapeutic approaches.

In this book, we start to describe the infrastructure/capability required for biomarker discovery and validation and then learn from experiences on biomarker discovery in pathologies related to endometriosis like cancer (endometriosis is a benign metastatic disease) and inflammatory diseases of the bowel, liver, brain, and cartilage (endometriosis is a chronic inflammatory disease). After highlighting the importance of patient centeredness in endometriosis care, we focus on epidemiology, risk factors, and genetic markers for endometriosis and provide insight into how OMICS and, more specifically, proteomics and transcriptomics have contributed to progress in this field. Extensive attention is given to the diagnostic performance of non- or semi-invasive tests for endometriosis based on (panels of) biomarkers in peripheral blood, peritoneal fluid, and eutopic endometrium. Recommendations of the World Endometriosis Research Foundation are summarized to illustrate the importance of internationally accepted standard operating

procedures for the collection, treatment, storage, and analysis of tissue samples and for detailed clinical phenotyping of these samples.

Two priorities emerge for the future on biomarker discovery in endometriosis.

Firstly, we need to move from innovation to validation. Indeed, in order to make progress for the benefit of patients, the most urgent task ahead is now to validate the diagnostic accuracy of any promising test prospectively in an independent symptomatic patient population with subfertility and/or pain without clear ultrasound evidence of endometriosis. This population should have a clinical indication for surgery (gold standard for diagnosis of endometriosis) and be divided into cases with laparoscopically and histologically confirmed endometriosis and controls with laparoscopically confirmed absence of endometriosis [2].

Secondly, more collaboration is needed between academic groups and industry to move from discovery via validation to clinical availability of biomarkers for endometriosis. Collaborative research efforts co-led by academia and industry, early on during clinical development of biomarkers, may accelerate validation of interesting biomarkers which is not sufficiently explored today. Most national/international research foundations focus so much on innovation and discovery and do not make funds available for validation. Both industry and academia should make an effort to prioritize resources and develop such partnerships for biomarker validation and development, building on their joint scientific and commercial excellence. In the end, patients will benefit from such collaborations, as long as they are scientifically sound and transparent [3].

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State of the Art

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