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Exome chip study provides novel insights into the genetics of pelvic organ prolapse

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Introduction and aim of the study: Pelvic organ prolapse (POP) is caused by a complex interplay of genetic and environmental factors. The aim of the study was to provide insights into the pathophysiological molecular pathways underlying the disease, by integrating the results from a large scale exome chip study with published genetic and expression data.

Materials and methods: Blood samples of 526 women with POP and 1911 control individuals were genotyped using an exome chip containing more than 240,000 exonic markers. We then conducted elaborate literature analyses of the top-ranked genes from the exome chip and genes implicated in POP through other evidence, including genetic association studies and expression studies in POP patients.

Results: The exome chip study yielded significant association between POP and mutations in 44 unique genes. The proteins encoded by 20 of these, together with 28 other POP candidate proteins and two POP-implicated microRNAs, fit into four molecular pathways: i.e. epithelial-mesenchymal transition, immune response activation, modulation of the extracellular matrix, and fibroblast survival and apoptosis. These four pathways were located in epithelial cells and fibroblasts of the urogenital tract, interact with each other and are regulated through signalling involving female sex hormones and the cytokine TGFB1.

Interpretation of results: The molecular pathways identified yield leads for existing drugs that could be repurposed or new disease-modifying treatments of POP.

Conclusions: Our findings provide detailed and novel insights into the genetically determined mechanisms that are involved in the pathogenesis of POP. This research has recently been submitted for publication.

http://dx.doi.org/10.1016/j.ejogrb.2017.01.043

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Fractional CO_2 laser effect on thick connective tissue of the vaginal wall of women with anterior vaginal prolapse: an ex-vivo study

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Introduction and aim of the study: POP occurs for a weakness/damage of the supporting connective structures. Cystocele is the most challenging condition. CO_2 laser is able to regenerate collagen fibres in the vaginal lamina propria. In this ex-vivo study we aimed to evaluate a possible regenerative effect in the anterior fascia of women with POP.

Materials and methods: We intra-operatively treated with CO_2 laser the anterior fascia before plication in 6 women with cystocele. A fascia biopsy was taken at different times after laser treatment; an untreated part was always taken as control. Controls and treated parts of the fascia were compared for production of new collagen

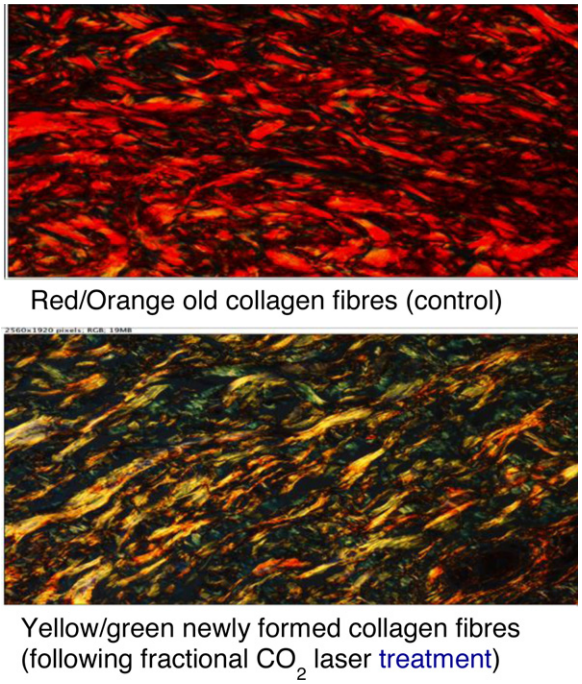

Fig. 1. Circularly polarized light microscopy. Microscopic features of collagen regeneration (Picrosirius Red stain) following fractional CO_2 laser treatment.