**Expression changes in pelvic organ prolapse: a systematic review and *in silico* study**

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**Supplementary Table S4** Literature data for shared up-regulated genes associated with prolapse-related conditions

| Gene symbol | Gene name | Number of sets[a] | Literature evidence | Proposed mechanism[b] | Reference |
|---|---|---|---|---|---|
| *ADAMTS1* | ADAM Metallopeptidase With Thrombospondin Type 1 Motif 1 | 2 | In microarray analysis, the *ADAMTS1* gene was up-regulated 4-fold in the vaginal wall from women with POP (n=5) in comparison with controls (n=5). | This gene is likely to be necessary for normal growth and organ morphology and function (http://www.genecards.org/). | Stratford et al., 2005 |
| *AGT* | Angiotensinogen | 2 | *AGT* M235T polymorphism was associated with mitral valve prolapse. | Angiotensin II can induce proliferation and differentiation of fibroblasts through the involvement of extracellular signal-regulated kinases proteins. Angiotensin-2 acts directly on vascular smooth muscle as a potent vasoconstrictor. | Chou et al., 2002; Fatini et al., 2008; Lung et al., 2008 |
| *CTSK* | Cathepsin K | 2 | Increased expression of CTSK has been reported in human myxomatous mitral valve disease (myxomatous degeneration is the pathological substrate of mitral valve prolapse). | CTSK is involved in osteoclastic bone resorption and may participate in the disorder of bone remodeling. It may play an important role in extracellular matrix degradation (http://www.genecards.org/). | Rabkin et al., 2001 |
| *EGR2* | Early Growth Response 2 | 2 | Defective aortic valves (AoVs) in *Egr2* -/- mice had features of human AoV disease, in particular excess of proteoglycan deposition and reduction of collagen fibres. | *EGR2* gene controls early myelination of the peripheral nervous system (http://www.genecards.org/). *EGR2* activation in interstitial cells of the AoV leads to *Col1a1* and *Col3a1* up-regulation. | Odelin et al., 2014 |
| *LIN28B* | Protein lin-28 homologue B | 2 | SNP linked to the *LIN28B* gene was associated with POP and stress urinary incontinence in the PheWAS Catalog. | The *LIN28* (*LIN28A* and *LIN28B*) genes may influence myelination in peripheral nervous system thus contributing to insufficient innervation with subsequent POP development. | Salnikova et al., 2016 |

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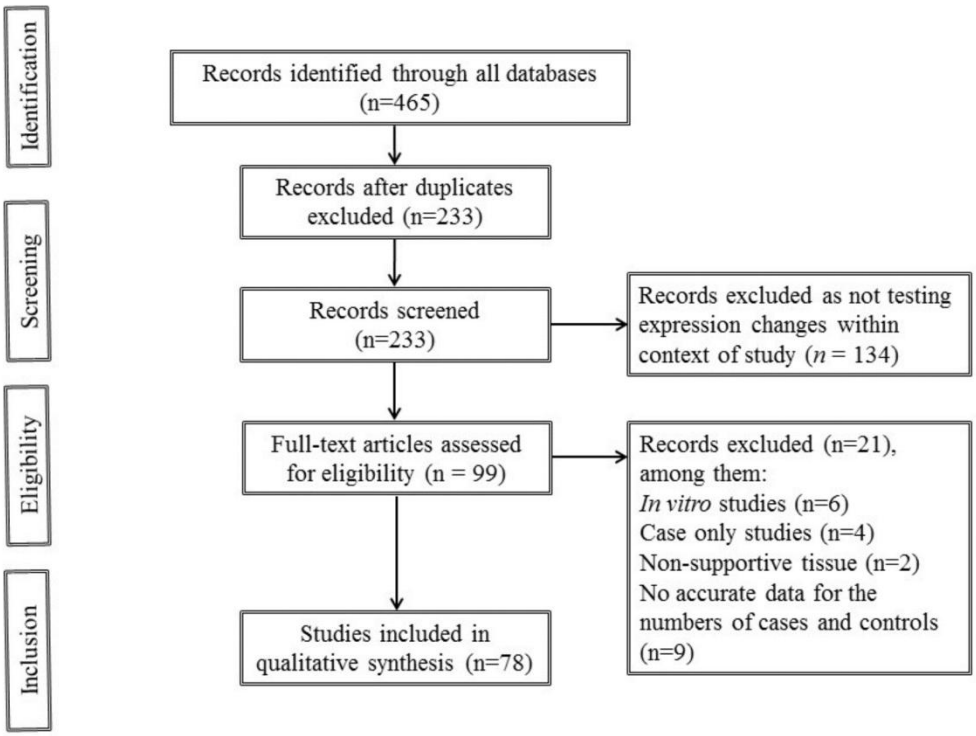
| *MMP19* | Matrix Metallopeptidase 19 | 2 | *MMP19* was over-expressed in specimens from patients with mitral valve prolapse (n=7) compared with control specimens (from non-beating heart-tissue donors, n=3). | MMP19 is involved in the breakdown of extracellular matrix in normal physiological processes including tissue remodeling. MMP19 is secreted as an inactive proprotein, which is activated upon cleavage by extracellular proteases (http://www.genecards.org/). | Greenhouse et al., 2016 |
| *MYH3* | Myosin Heavy Chain 3 | 2 | *MYH3* was 3.2 times over-expressed in the rectus abdominus muscle of patients with POP (n=15) relative to controls (n=13). | *MYH3* is nvolved in muscle contraction (http://www.genecards.org/). | Hundley et al., 2008 |
| *NFIL3* | Nuclear Factor, Interleukin 3 Regulated | 4 | Approximately 20 and 50% of *Nfil3-/-* mice develop rectal prolapse 20 and 36 wk. of age, respectively. | *Nfil3-/-* mice develop microbiota-dependent spontaneous colitis linked to defects in innate immune response. | Kobayashi et al., 2014 |
| *NLRP3* | NLR Family Pyrin Domain Containing 3 | 2 | NLRP3 inflammasome was upregulated in colonic mucosa of *IL-10-/-* mice and Crohn's patients. By 6 mo of age all *IL-10-/-* mice had intestinal inflammation and rectal prolapse. | *NLRP3* plays a crucial role in innate immunity and inflammation. | Liu et al., 2016; McCafferty et al., 2000 |
| *SERPINE1* | Serpin Family E Member 1 | | *SERPINE1* significantly increased in stroma from menopausal women with POP (n=8) compared with controls (n=5). | SERPINE1 inhibits active metalloproteinases (MMPs) and suppresses elastic fiber degradation. | Budatha et al., 2013 |
| *THBS4* | Thrombospondin 4 | 2 | *THBS4* was over-expressed in specimens from patients with mitral valve prolapse (n=7) compared with control specimens (from non-beating heart-tissue donors, n=3). | THBS4 is an adhesive glycoprotein that mediates cell-to-cell and cell-to-matrix interactions. It contributes to local signaling in the developing and adult nervous system (http://www.genecards.org/). | Greenhouse et al., 2016 |

[a]Number of datasets under study, in which the genes were up-regulated. [b]The mechanisms were proposed in cited articles, otherwise specified.

Supplementary Figure S1. Flow diagram of the literature search for the studies of POP-related expression changes



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