Sphingosine 1-phosphate (S1P) pathway in uterine fibroids

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Introduction

- **Uterine fibroids** are characterized by increased proliferation of disordered smooth muscle cells, altered extracellular matrix (ECM) deposition, and enhanced responsiveness to sex steroid hormones.
- **Sphingolipids** are bioactive signaling mediators, modulating a variety of cellular processes, including cell proliferation and suppression of programmed cell death. **Sphingosine 1-phosphate (S1P)** is generated by the enzyme sphingosine kinase (SK), whereas the catabolism is mediated by S1P lyase (SPL) and by two distinct specific S1P phosphatases (SPP). A complex cross-talk between S1P signaling and growth factors has been observed, promoting multiple biological actions such as proliferation and fibrosis.

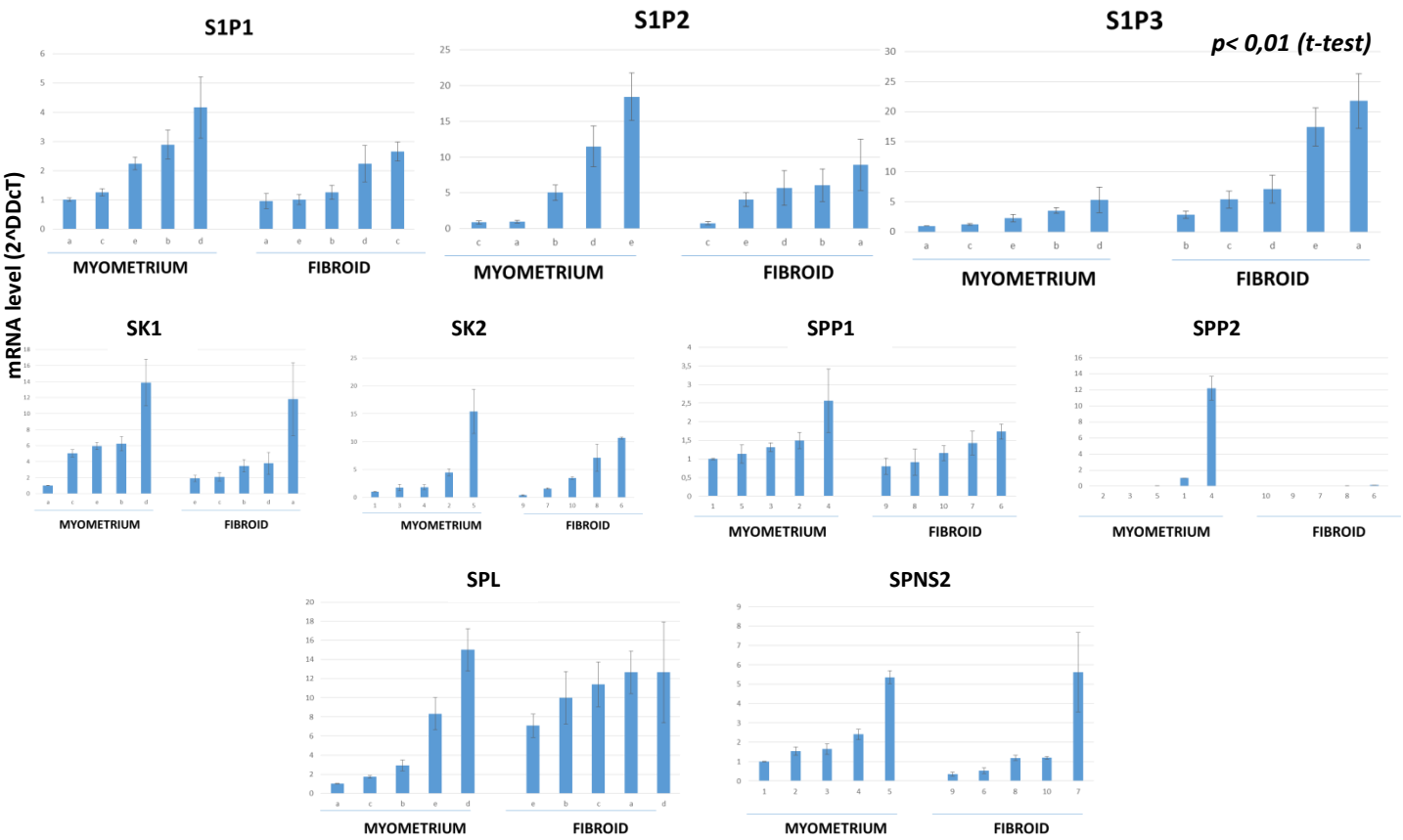
Aim of the study

To investigate whether S1P signaling axis is deregulated in human uterine fibroids. In particular, we compared the expression of genes related to S1P metabolism (SK, SPL, SPP) and signaling (S1P receptors and S1P specific transporter SPNS2) between fibroids and healthy myometrium.

Materials and Methods

Immediately following hysterectomy, 10 tissue samples (5 human uterine fibroids and 5 human control myometrium) were dissected and RNA was extracted. Total RNA (1 µg) was reverse transcribed and quantification of mRNA was performed by real-time PCR. Each measurement was carried out in triplicate, by simultaneous amplification of the target sequence together with the housekeeping gene beta actin. The 2-ΔΔCT method was applied as a comparative method of quantification and data were normalized to beta actin. Statistical analysis was performed using Student's t test.

Results



Conclusion

An altered S1P metabolism and signaling contribute to smooth muscle cells proliferation and survival observed in uterine fibroids. Besides, S1P pathway seems to be involved in fibrosis induction, through the remodeling of S1P receptors expression profile.