SYNOVIM ANGIOGENESIS IN OSTEOARTHRITIS: A NEW THERAPY TARGET FOR CHONDROITIN SULFATE

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PURPOSE

Angiogenesis and inflammation are closely integrated process. Chondroitin sulfate (CS) is a symptomatic slow acting drug for OA. The mechanisms underlying these effects remain poorly understood. This work aimed to study

• the pro inflammatory and pro/anti angiogenic status of synovium
• the effect of CS on angiogenic factors expression by synovial cells (SC)

METHODS

SC culture (3 to 5 synovial specimen), P4, 5 or 24 h incubation
• Without IL-1β (basal) + CS (0, 10, 50, 200 µg/ml)
• With IL-1β (1ng/ml) + CS (0, 10, 50, 200 µg/ml)
• Pro angiogenic genes expression (RT PCR): VEGF, basic Fibroblast Growth Factor (bFGF), Nerve Growth Factor (NGF), Matrix Metalloproteinase (MMP)-2, angiopoietin (ang)-1
• Anti angiogenic genes expression (RT PCR): TSP-1 and -2, Vascular Endothelial Growth Inhibitor (VEGI)

RESULTS

1. An increase of pro inflammatory and pro angiogenic status is observed in SCI

| Inflammation | Pro | IL-6 | 419 ± 109 | ***
|--------------|-----|------|-----------|-----
|              | IL-8| 730 ± 309 | ***

| Angiogenesis | Pro | VEGF | 134±16 | ***
|--------------|-----|------|--------|-----
|              | Anti| TSP-1| 66±15  | ***

Table 1: Production of IL-6, 8, VEGF and TSP-1 of SCNI and SCI. Results are expressed as % of production of SCNI (means ± SEM).

2. IL-1β stimulates pro angiogenic genes expression
3. * IL-1β stimulates anti angiogenic genes expression after 5 h
   * IL-1β inhibits anti angiogenic genes expression after 24 h

![Fig 1: Effect of IL-1β on pro and anti angiogenic genes expression. Results are expressed as % of basal expression (means ± SD).](image)

4. The inhibiting effect of IL-1β (24 h) on anti angiogenic factors expression (TSP-1 and VEGI) was counteracted by CS

![Fig 2: Effect of CS on anti angiogenic factors expression after 24 h of treatment. Results are expressed as % of expression obtained in the absence of CS (means ± SD).](image)

CONCLUSIONS

• Synovium inflammation is associated with an imbalance between pro and anti angiogenic factors production.
• IL-1β is a key inflammatory mediator capable of inducing this pro angiogenic imbalance.
• The basal expression of pro and anti angiogenic genes expression and the IL-1β stimulated pro angiogenic genes expression are not affected by CS
• CS trends to normalize the IL-1β-induced angiogenic response in OA SC. This could constitute a new mechanism of action of this drug, modulating the molecular mechanisms underlying the synovium angiogenesis in OA. These results also contribute to understand the molecular mechanism of angiogenesis in OA.