P593

TERMIS EU-Chapter

PALMA DE MALLORCA

21-24 APRIL / SPAIN

Can spinal fusion for the elderly be improved? BMP2, L51P, and the EP4 agonist KMN159: synergistic osteogenesis in human annulus fibrosus cells

Benjamin Gantenbein[1], Shuimu Chen[1], Xinggui Tian[2], Laura González-Blanco[1,3], Oreste Gualillo[3], Stefan Zwingenberger[2], Christoph E. Albers[1,4] and Sonja Häckel[1,5]

[1]Department of Orthopaedic Surgery & Traumatology, Inselspital, Bern Faculty of Medicine, University Hospital, University of Bern, Bern, Switzerland
[2]Center for Orthopaedic, Trauma Surgery and Rehabilitation Medicine, University Medicine Greifswald, Greifswald, Germany
[3]IDIS (Instituto de Investigación Sanitaria de Santiago), The NEIRID Group, Santiago University Clinical Hospital, Santiago de Compostela, Spain
[4]Orthopädie Sonnenhof, KLG, Bern, Switzerland, [5]Graduate School for Health Sciences (GHS), University of Bern, Bern, Switzerland

INTRODUCTION

- Low back pain (LBP) is a significant global burden and is associated with the degeneration of the spine and human intervertebral discs (hIVD) [1].
- Spinal fusion surgery is widely used to restore spinal alignment and stability; however, achieving successful fusion remains challenging, particularly in older patients, often resulting in suboptimal outcomes [2].
- Minimally invasive biological strategies may improve fusion by enhancing osteogenesis. Factors such as bone morphogenetic protein-2 (BMP2), its analog L51P, and KMN159, a prostaglandin E2 receptor 4 agonist, have been shown to modulate osteogenic differentiation and inflammation [3].
- The aim of this study is to investigate the potential of these factors to promote IDV fusion by inducing osteogenic differentiation in human annulus fibrosus cells (AFCs).

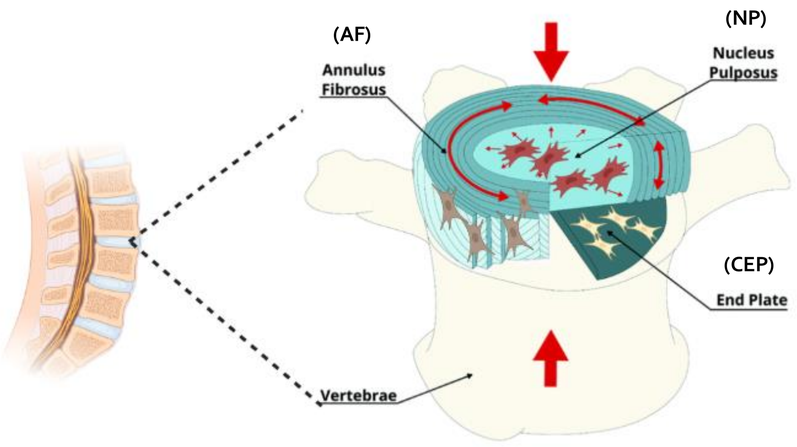
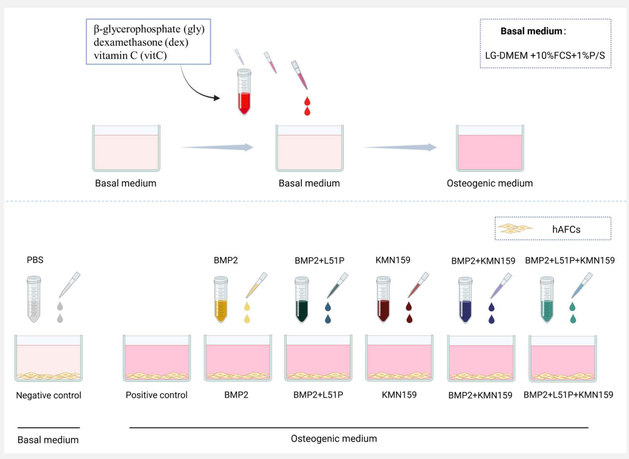


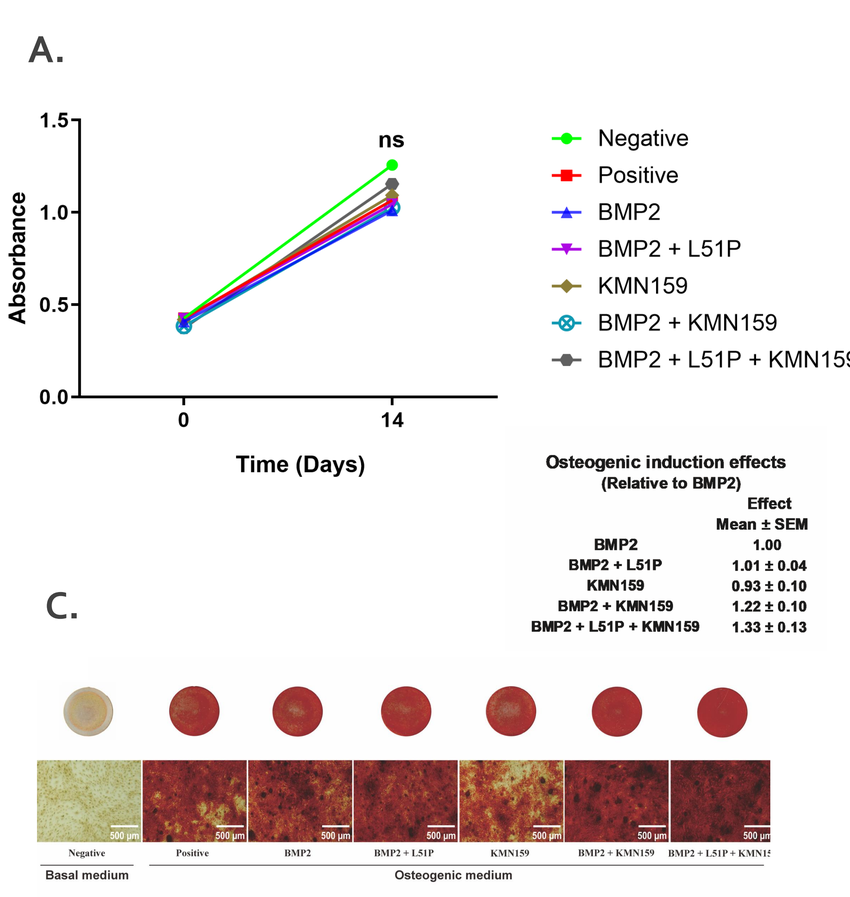
Figure 1. Main cell types in IVD.

MATERIAL & METHODS

- Primary human AFCs were isolated and cultured from patient samples (n = 11).
- Cells were stimulated with BMP2 (100 ng/mL), L51P (100 ng/mL), and KMN159 (400 ng/mL), alone or in combination, for up to 21 days.
- Cell viability and ALP activity were assessed at day 14, and matrix mineralization at day 21 by Alizarin Red staining, as previously described Chen et al. [4].
- Osteogenic differentiation (days 7, 14, 21) was evaluated by gene expression (ALP, RUNX2, BGLAP, SPP1, SP7, COL1).
- BMP antagonists (Noggin, Gremlin-1, Chordin) were analyzed by qPCR.
- Statistical analysis was performed using t-test or ANOVA ($p < 0.05$).



RESULTS



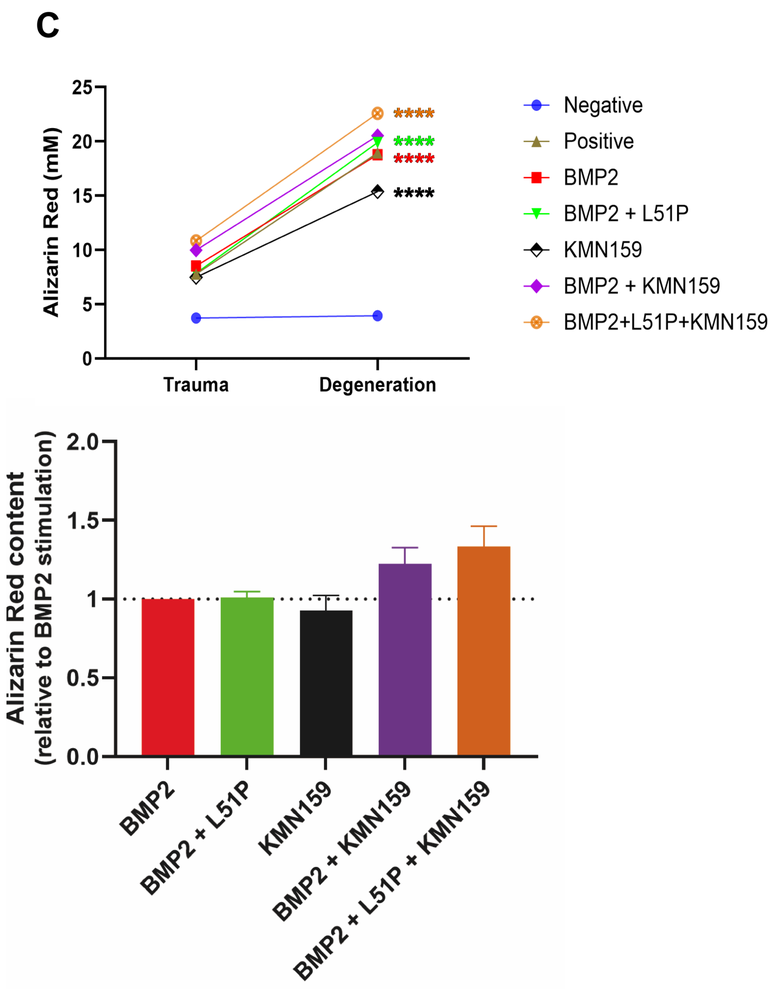


Figure 2. (**A**) Cell viability of human AFCs assessed by XTT assay after 14 days showed increased viability in all groups compared to Day 0, with no significant differences between treatments ($p > 0.05$; $n = 4$). (**B**) ALP activity after osteogenic induction was highest in the triple combination (>5-fold vs BMP2), with lower increases in BMP2 + KMN159 (2.7-fold) and BMP2 + L51P (1.1-fold; BMP2 = 1.00). (**C**) Alizarin red staining and quantification after 21 days demonstrated increased calcium deposition, with the triple combination showing the highest mineralization (1.33-fold vs BMP2). Data are presented as mean ± SEM.

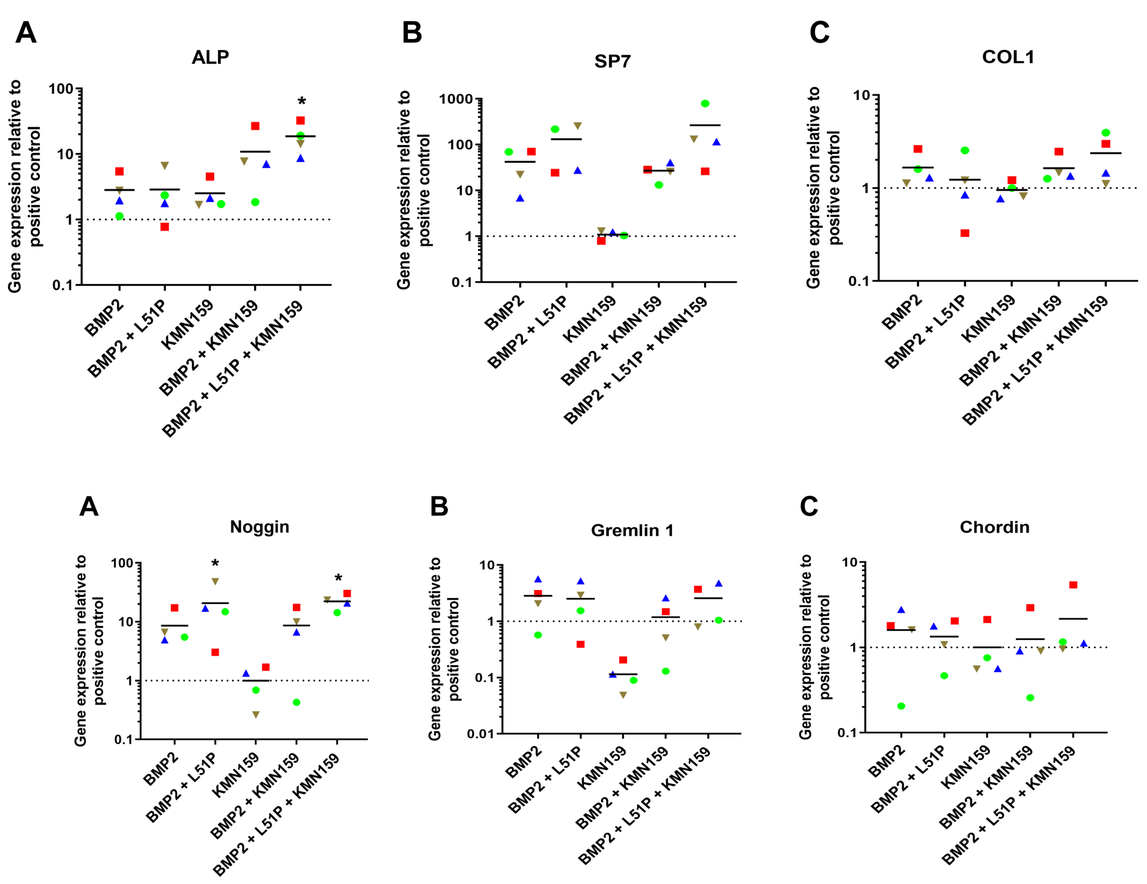


Figure 3. qPCR analysis of bone-related gene expression in human AFCs. ALP, SP7, and COL1 expression were highest in the triple combination (BMP2 + L51P + KMN159), with significant upregulation of ALP ($p < 0.05$). KMN159 alone had minimal effects. Data are presented as mean ($n = 4$).

Figure 4. Gene expression of BMP2 antagonists in AFCs following different treatments. KMN159 alone had minimal effects, while BMP2-containing groups increased expression, highest in the triple combination ($p < 0.05$; $n = 4$).

CONCLUSION

- The combination of KMN159, BMP2, and L51P promotes osteogenic differentiation in human AFCs.
- This approach enhances osteogenesis without removing the IVD.
- Minimally invasive biological strategies may improve spinal fusion outcomes and offer new therapeutic options for patients with low back pain.

REFERENCES

1. James et al., 2018. The Lancet 392(10159): 1789-1858
2. Veronesi et al., 2022. J Clin Med 11.
3. Owen et al., 2020. Gene 748:144668.
4. Chen et al., 2026. Eur Spine J. 1-11.

Funding
S.C. was supported by the China Scholarship Council (No. 202208170027). S.H. was supported by the Swiss Society of Orthopaedics (SGOT), and by the Spark program of the Swiss National Science Foundation no. CSRK3_237950 (https://data.snf.ch/grants/grant/237950,, and by the German Spine Society (DWG) Basic Science Grant.

Contact:
benjamin.gantenbein@unibe.ch