

## Migration of mesenchymal stem cells into degenerative intervertebral discs

Sebastian Wangler<sup>1,2</sup>, Marianna Peroglio<sup>1</sup>, Zhen Li<sup>1</sup>, Ursula Menzel<sup>1</sup>, Lorin M. Benneker<sup>3</sup>, R. Geoff Richards<sup>1</sup>, Mauro Alini<sup>1</sup>, Sibylle Grad<sup>1</sup>

<sup>1</sup> AO Research Institute Davos, Davos, Switzerland, <sup>2</sup>Graduate School for Cellular and Biomedical Sciences, University of Bern, Switzerland <sup>3</sup> Inselspital, Bern, Switzerland

**Introduction:** The repair capacity of a traumatic or degenerative intervertebral disc (IVD) is very low which is causing chronic low back pain. Attraction of mesenchymal stem cell (MSC) is a potential mechanism for in situ regeneration and might present a novel treatment strategy. The present project aims to characterize the MSCs which are migrating into a degenerative IVD.

**Methods:** MSCs were isolated from human bone marrow. IVDs from bovine tails were loaded in a whole organ culture bioreactor to simulate a degenerated IVD. The culture medium was collected as “conditioned medium”, containing the signaling proteins released by the IVDs.

**(1) In vitro experiment:** MSCs were separated in subpopulations containing or not the surface protein CD146. The sorted subpopulations were placed on a membrane. Conditioned medium was put under membrane in order to attract the cells. After 16 h, the number of migrated cells was counted by automated cell counter.

**(2) IVD culture experiment:** CD146+ and CD146- sorted MSCs were labeled with red and green fluorescent dyes, respectively. Each population was placed on a separate degenerative bovine IVD. After 5 days, IVDs were fixed, cut in sagittal sections, and the number of migrated cells was counted by fluorescence microscopy.

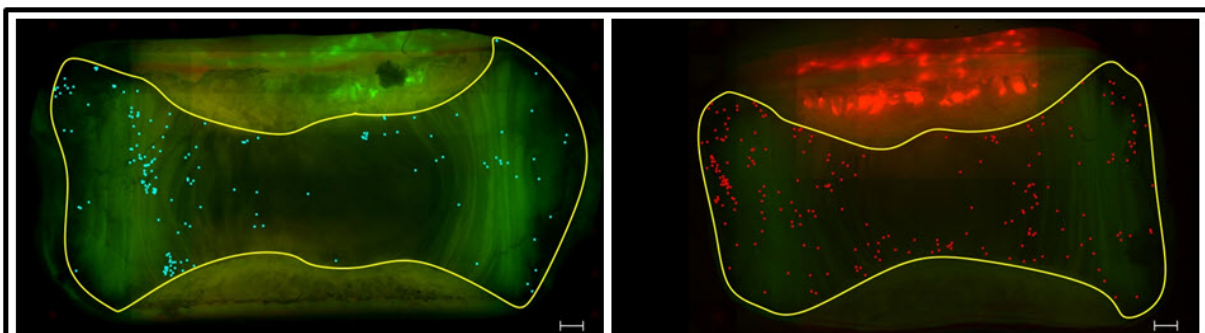
### Results

**(1)** The proportion of MSCs migrating towards disc conditioned medium was significantly higher for CD146+ (22.5 % migrated cells) compared to CD146- (15.7 % migrated cells;  $p < 0.01$ ) sorted MSCs.

**(2)** The organ culture experiment confirmed that CD146+ MSCs had a superior migration potential toward induced-degenerative disc tissue ( $179.6 \pm 29.6$  cells/cm<sup>2</sup>) when compared to CD146- MSCs ( $99.2 \pm 4.3$  cells/cm<sup>2</sup>) (Fig. 1).

### Conclusion

CD146 positive MSCs showed a superior migration potential compared to CD146 negative MSCs both in vitro and in whole organ culture. Further studies will assess if the enhanced expression of CD146 is associated with an increased regenerative potential of this sub-population.



**Fig. 1:** Combined red and green fluorescent image of migrated MSCs in a sagittal section of bovine IVDs. Left: CD146- MSCs (blue); right: CD146+ MSCs (red). The IVD region without endplates is marked with a yellow line. Scale bar = 1 mm.