The role of ALDH<sup>br</sup> BCSCs as prognostic markers and therapeutic targets in breast cancer

Introduction:

- The CSC theory proposes that CSCs are able to establish themselves, drive tumorigenesis giving rise to all cancer cell types, induce metastasis and recurrence, because of their self-renewal, differentiation and chemotherapy/radiotherapy resistance abilities.
- Isolation of CSCs and targeting therapies against them are needed to overcome cancer.
- ALDHs are CSC markers and ALDH<sup>br</sup> CSCs selects for poor prognosis cancers.
- ALDHs are involved in the RA signalling, the self-protection against oxidative stress and the chemotherapy/radiotherapy resistance of CSCs.

Objectives:

1. To study the role of ALDHs in BCSCs.
2. To assess ALDH<sup>br</sup> BCSCs as prognostic markers in breast cancer.
3. To assess ALDH<sup>br</sup> BCSCs as therapeutic targets in breast cancer.

Results:

Transcriptional and post-translational regulation of ALDHs in BCSCs

The role of ALDHs in the RA signalling pathways of BCSCs

The role of ALDHs in the self-protection against oxidative stress of BCSCs

The therapeutic target value of ALDH<sup>br</sup> BCSCs

Conclusions:

1. ALDHs are BCSC markers tightly related with the behaviour of BCSCs, where they play a functional role in the RA-signalling pathways, the self-protection against oxidative stress and the chemotherapy/radiotherapy resistance.
2. ALDH<sup>br</sup> BCSCs are poor prognosis markers in breast cancer.
3. ALDH<sup>br</sup> BCSCs are possible future therapeutic targets to overcome breast cancer.

- ALDH1A3<sup>br</sup> BCSCs are the best ALDH markers to predict prognosis.
- ALDH1A3<sup>br</sup> BCSCs are poor prognosis markers.
- Further research is needed to adjust their prognostic value.
- Further research is needed regarding the best combination of markers.
- Further research is needed regarding the distinction between ALDH<sup>br</sup> BCSCs and ALDH<sup>br</sup> normal breast SCL.
- The combination of retinoic acids and epigenetic modifiers is the most promising therapy.
- Targeting against the Notch and the TGFβ signalling of ALDH<sup>br</sup> BCSCs inhibits their BCSC behaviour.
- Direct targeting against ALDH<sup>br</sup> BCSCs inhibits BCSC behaviour.
- Further research is needed on the previously described targets and on the targeting of other ALDH-regulatory and functional signalling pathways.
- Further research is needed regarding the distinction between ALDH<sup>br</sup> BCSCs and ALDH<sup>br</sup> normal breast SCL.