17-DMAG DISTURB THE SUBCELULLAR LOCALIZATION BETWEEN HSP90α AND HSP90β WITH β -CATENIN AND DETERMINATES THE CELL MIGRATION CAPACITY IN CERVICAL CANCER CELLS

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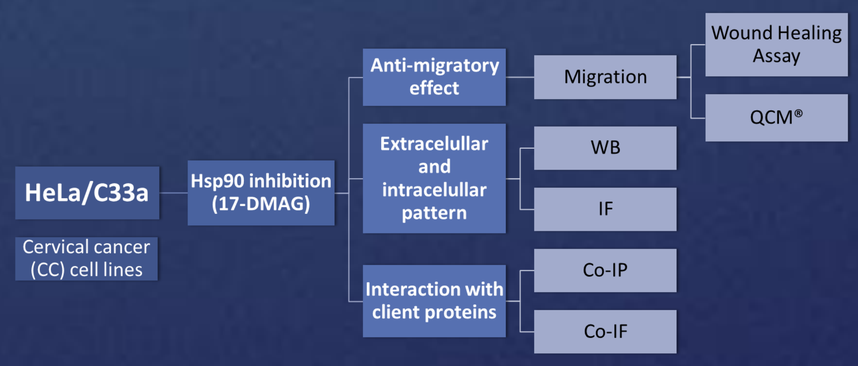
INTRODUCTION

The Hsp90 sub-family is composed of two major cytosolic isoforms in mammalian cells, Hsp90α and Hsp90β. Specific functional role of each isoforms remains poorly understood, particularly their involvement in diseases such as in cancer. In this regard, we recently demonstrated that Hsp90α and Hsp90β isoforms have a differential role on the Akt kinase activity. In turn, Akt is a major positive regulator of β-catenin signaling pathway, playing a key role in the transcription of genes involved in proliferation and cell migration in both normal and cancer cells. To date, several pharmacological inhibitors of Hsp90, including to 17-DMAG, have been tested for the treatment of cancer, however, the efficacy in their antitumor effects is limited. In this respect, we propose that the different expression and subcellular localization of the Hsp90 isoforms could be responsible of this poor efficacy.

OBJECTIVE

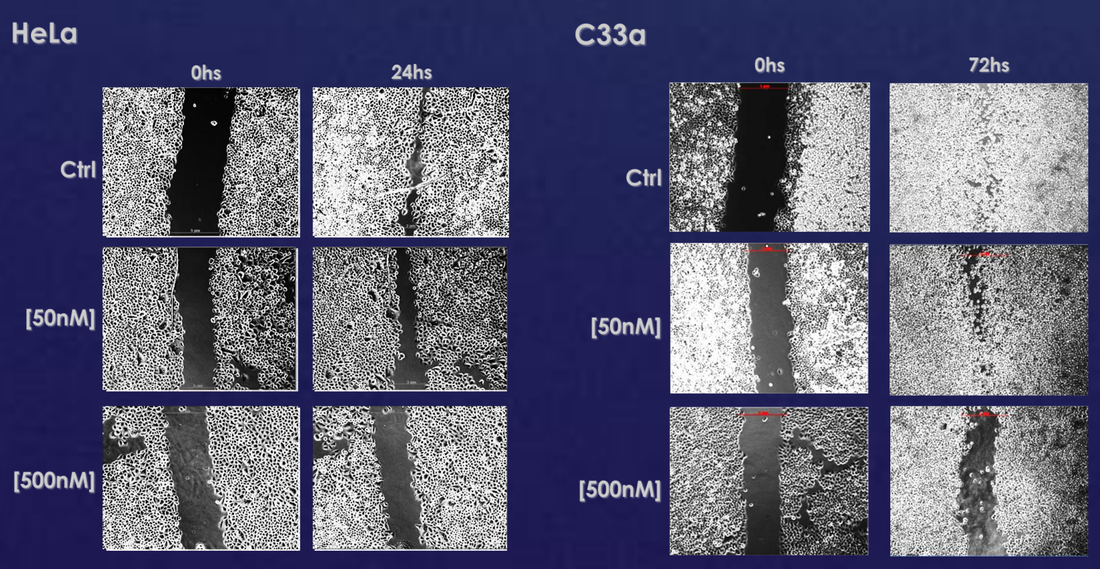
To evaluate the role of the subcellular localization of Hsp90α and Hsp90β on cell migration mediated by Akt/β-catenin, in cervical cancer cells treated with 17-DMAG.

METHODOLOGY

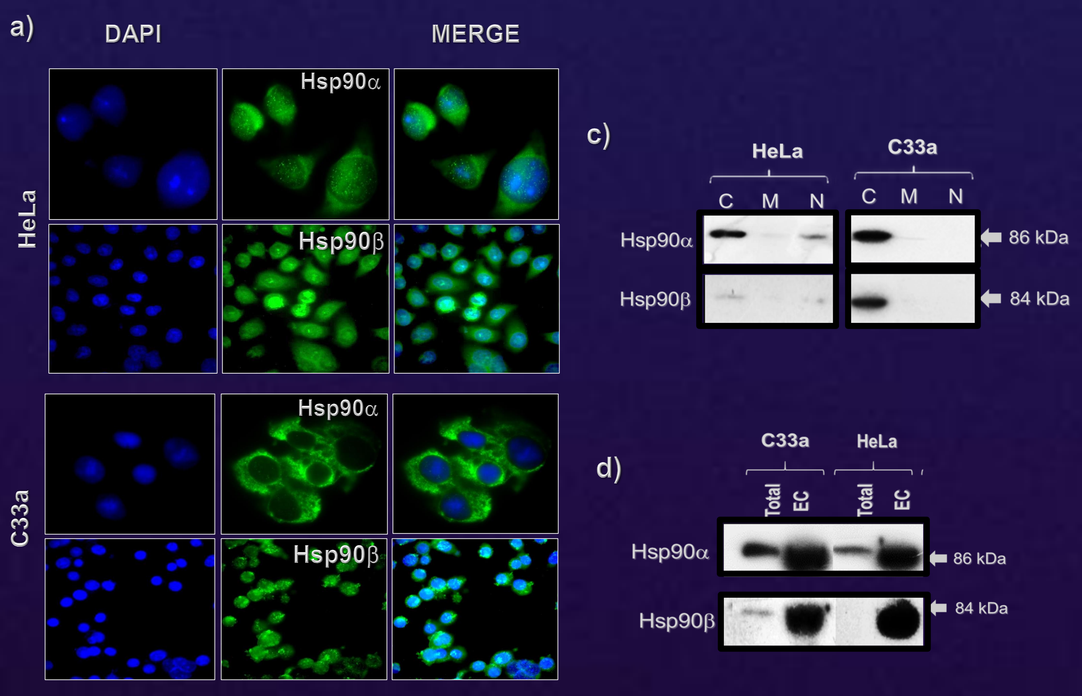


RESULTS

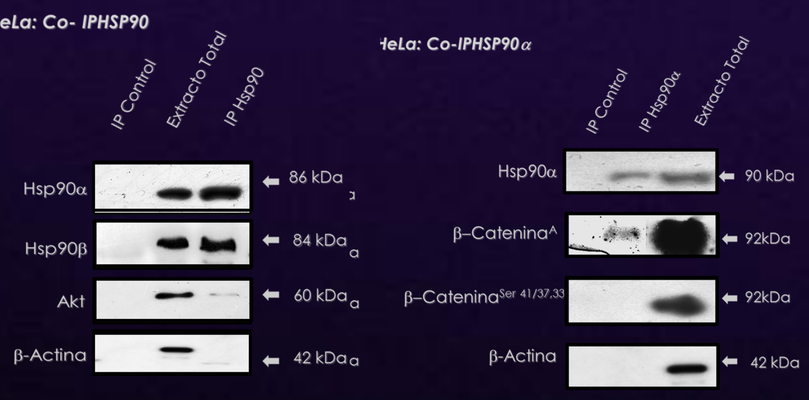
1) Anti-migratory effect of inhibition of Hsp90 with 17-DMAG on CC cell lines



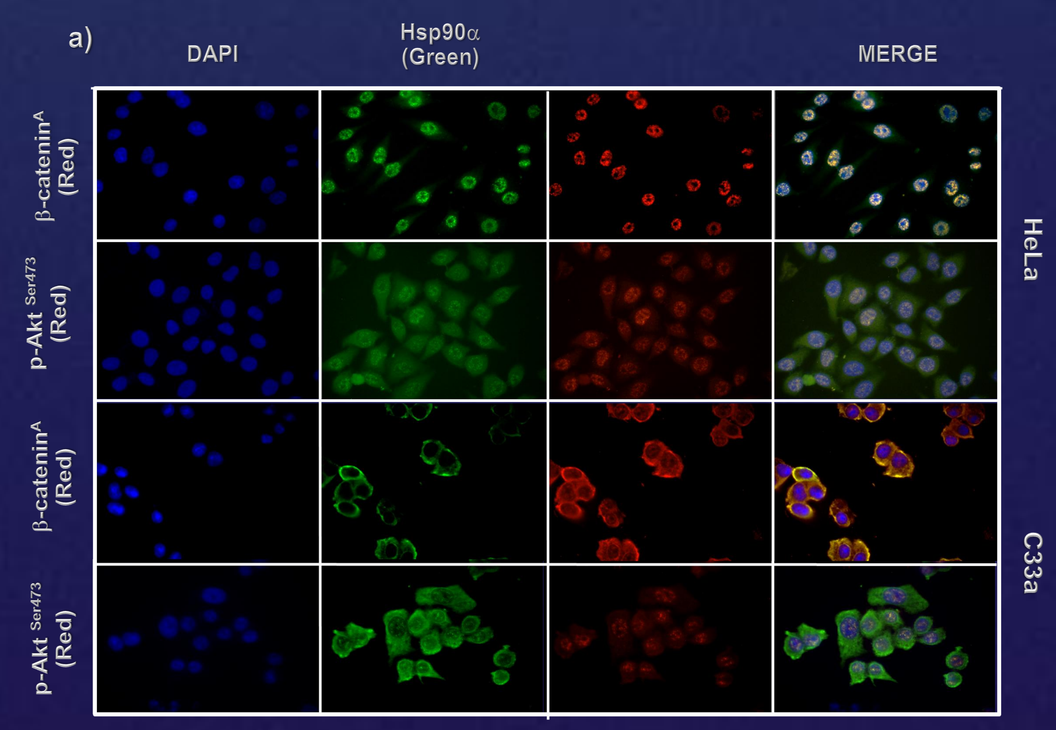
2) Expression and localization pattern of Hsp90α and Hsp90β on CC cell lines



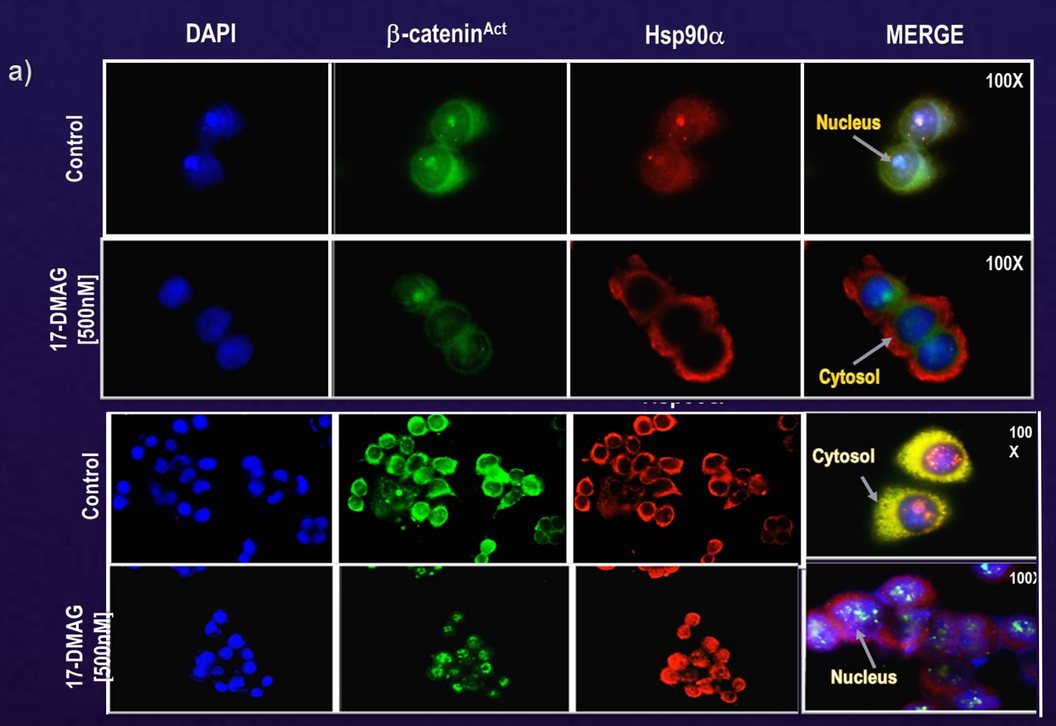
3) Interaction pattern of Hsp90α and their client proteins Akt/β on HeLa cell line



4) Co-localization pattern of Hsp90α and their client proteins Akt/β in CC cell lines,



3) Effect of inhibition of Hsp90, promotes a change in expression and localization profile



CONCLUSIONS

For the first time, we described differential role of the nuclear and subcellular localization of Hsp90α and Hsp90β on cell migration, associated to the activation of β-catenin in cervical cancer cells.

Treatment with 17-DMAG not only disturbes expression profile of Hsp90α but also its localization and nuclear co-localization with β-catenin. Interestingly we found association between upregulation and ci-locallization of Hsp90α and β-catenin with sensitivity to 17-DMAG.