The role of dipeptidyl peptidase III in mammalian physiology

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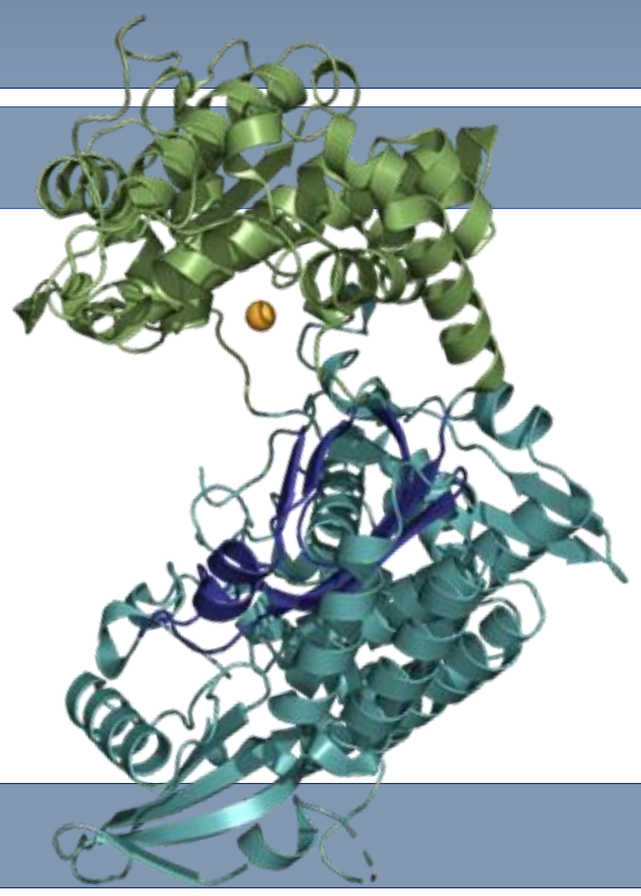
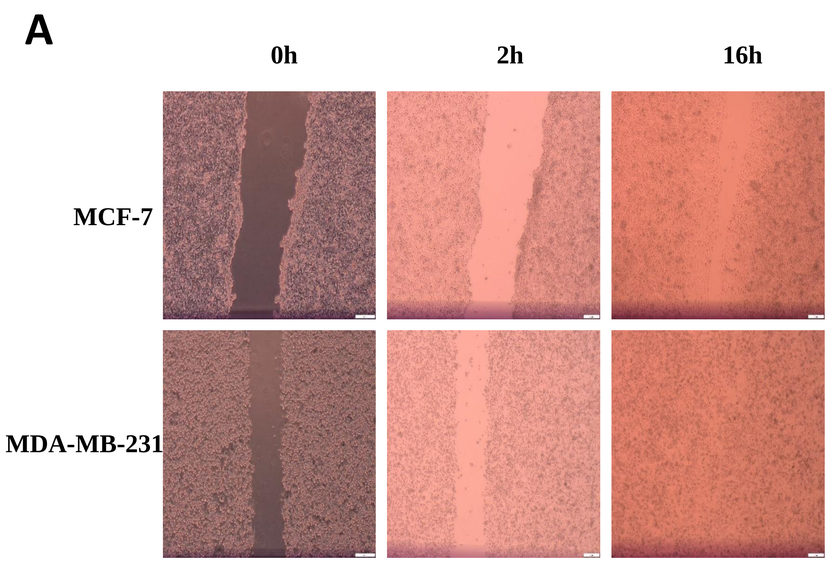
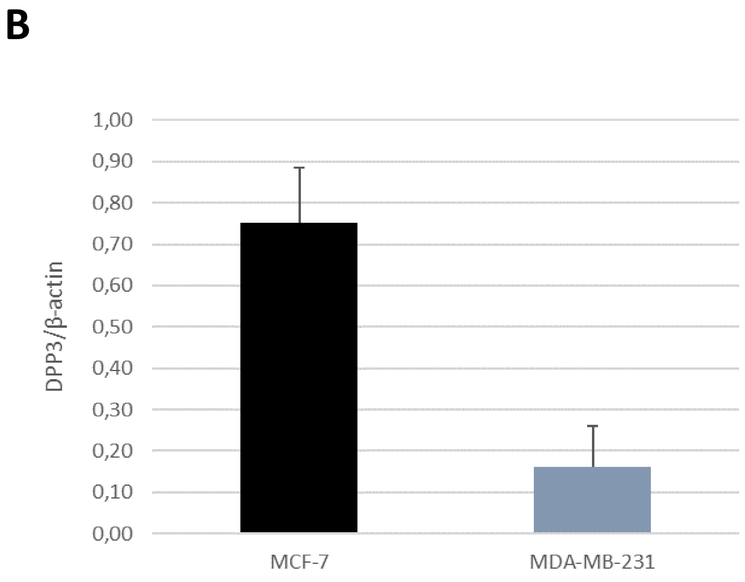
INTRODUCTION

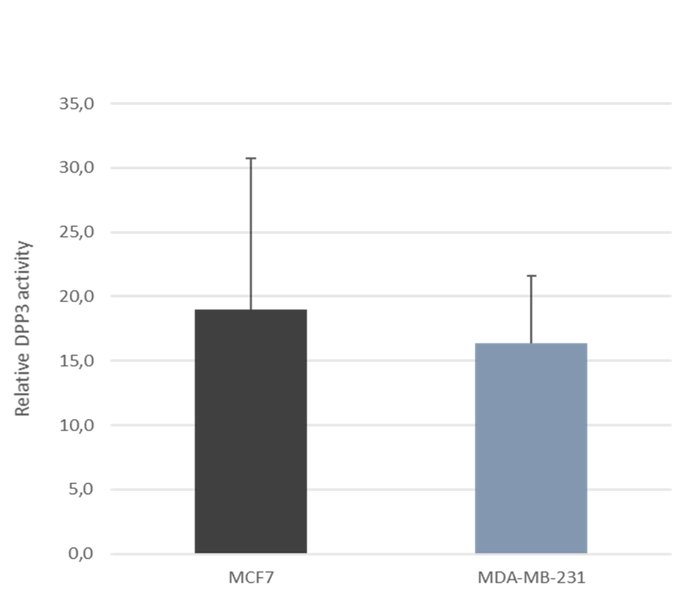
Dipeptidyl peptidase III (DPPIII), the sole member of the M49 family of metalloproteases with the mass around 80-85 kDa, is a zinc-dependent aminopeptidase that specifically cleaves dipeptides at the N-terminus of oligopeptides 4-10 residues long [1]. DPPIII was first isolated from the bovine anterior pituitary gland in 1967 after which its isolation from a number of other tissues from bacteria to eukaryotes began [2]–[8]. DPPIII is primarly a cytosolic protein [8]–[10] and is associated with important physiological functions and pathological processes [4], [7], [11]–[15]. The main goal of this project is to determine the role of dipeptidyl peptidase III (DPPIII) in mammalian physiology with an emphasis on breast cancer. Most recent publications have shown that elevated levels of DPPIII can serve as an indicator of a poor prognosis in the development and treatment of breast cancer. In addition, elevated DPPIII levels have also been reported to reduce the life expectancy of breast cancer patients[16]. Therefore, using modern methods we will address the basic questions concerning of the role of DPPIII in mammalian physiology and explore whether DPPIII can serve as a new target in early detection and treatment of breast cancer.

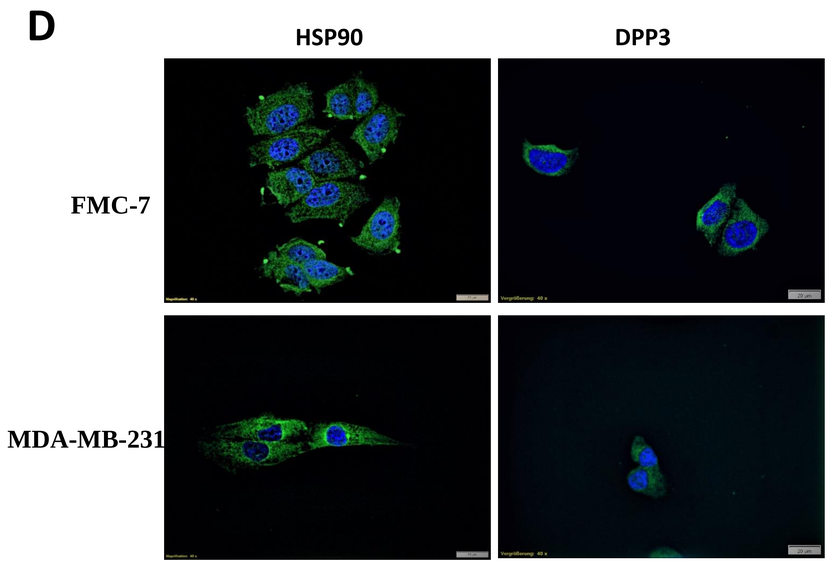


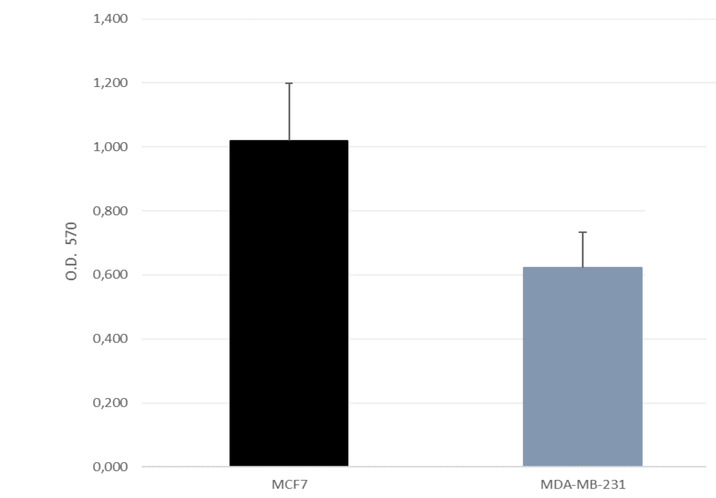
PRELIMINARY RESULTS

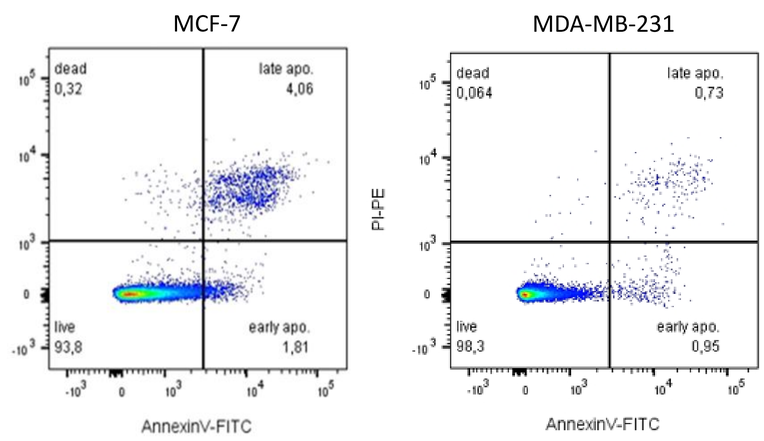












Characterization of MCF-7 and MDA-MB-231 breast cancer cell lines: (A) Wound-healing assay shows different rate of migration thus confirming greater invasiveness of MDA-MB-231 cell line **(B)** basic level of DPPIII protein level is higher in MCF-7 cell line **(C)** relative DPP3 activity **(D)** immunofluorescence employed to check localization of DPPIII in cell lines **(E,F)** MTT assay together with flow cytometry show higher metabolic activity in MCF-7 cell line and no change in apoptosis between two cell lines.

SIGNIFICANCE OF THE PROJECT

The relevance of the project lies in the fact that it will elucidate the role of DPPIII in human pathologies such as cancer, acute shock syndromes and inflammatory diseases. Based on this knowledge, we will explore whether DPPIII presents a new therapeutic target for the treatment of a variety of diseases that are related to the physiologic role of the enzyme. Thus, the study of DPPIII will also pave the way for new therapeutic intervention strategies with a potential impact on public health issues.

References
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