I. SUMMARY

Characterization of Human Teneurin-4 Transcript in Ovarian and Breast Cancer -Derived Cell Lines

Teneurins are transmembrane glycoproteins encoded by ODZ genes. Teneurins are a unique protein family conserved from flies and worms to human and are mainly expressed in the developing and adult nervous system where they are thought to be crucial for neurogenesis and axon-guidance. Teneurins are also expressed outside CNS where they have been proposed to play a role in morphogenesis and cell migration. Vertebrate teneurin expression pattern has been studied most extensively in mice and chicken, however still very little is known about their biological function and mechanism of action in humans.

Moreover, experimental data concerning the molecular structure of vertebrate teneurins transcripts is scarce, and human ODZ4 messenger has not been subject to a detailed characterization before.

Furthermore, recent studies have evidenced that some ODZs, specifically ODZ2 and 4, could be involved in tumor development in a still unclear mode. To this respect, in our preliminary study we demonstrated the expression of ODZ2 in human ovarian and breast cancer-derived cell lines by RT-PCR.

Therefore, in this thesis work we have evaluated the expression of ODZ4 in human ovarian and breast cancer-derived cell lines by RT-PCR. As a result, we have characterized two partial ODZ4 full-length messengers expressed by these cell types. The exon-expression pattern analysis indicates that these ODZ4 transcripts can be differentiated by the presence of an insert region corresponding to a non-adjacent genomic sequence that lies between exons 6 and 7. Additionally, the number of exons expressed differs depending on the type of cell line analyzed, even though they may derive from the same tissue type. Further, exonic deletions were not detected along these ODZ4 transcripts but many other truncated splice variants

were observed.

This study intends to generate new molecular information necessary for the elucidation of the functional role of ODZ4 in human cancer.