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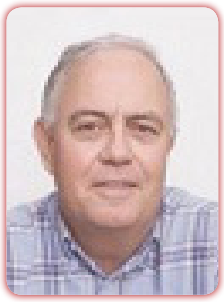

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Gonadotropin releasing hormone agonists (GnRH-A) induce direct apoptotic effects upon the human prostate cancer DU-145 cells: Potential avenue for treatment

GnRH is the primary and a key hormone which controls the reproductive system in all vertebrates. GnRH binds to its cognate receptor (GnRHR) in pituitary gonadotropes to regulate the synthesis and secretion of the gonadotropins: Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH). LH and FSH in turn control gametogenesis and sex hormone production in the gonads. GnRHRs are present not only in pituitary gonadotropes but also in some sex-hormone dependent cancers, including prostate cancer. Prostate cancer which is also known as Carcinoma of the Prostate (CaP) is the second death causing cancer in the western world. While GnRH secretion in a pulsatile manner regulates normal reproductive functions, application of GnRH agonists (GnRH-A) or antagonists in a continuous manner disrupts this regulation. As a result, the continuous application of GnRH-A causes desensitization of the GnRHR in the pituitary, termination of production and secretion of LH and FSH which in turn causes reduction in testosterone secretion, known as Chemical Castration. This is the basis for the clinical use of GnRH analogs in prostate cancer. However, in later stages, CaP may become hormone-independent, therefore, treatment with GnRH-A in a continuous manner is not beneficial for these cancers. Hence, a novel potential treatment for hormone-independent CaP is required and so it was very important to us to investigate this issue and explore a potential beneficial treatment. Indeed, direct apoptotic effects of GnRH-A upon hormone-independent CaP cells (DU-145) has been described, but the magnitude of the effect was not sufficient and potentiation of the effect was required. In this presentation, we will describe our efforts to elucidate cross-talks between the GnRHR and other GPCRs with the basic aim to potentiate the apoptotic effect of GnRH-A. Since there is no cure to advanced hormone resistant CaP, our work may open a new vista for the development of a combination therapy.

Biography

Zvi Naor is an Emeritus Professor in the Department of Biochemistry and Molecular Biology at Tel Aviv University, Israel. He has published over 150 papers on GnRH receptor signaling. He is a recognized expert in the field of endocrinology, reproductive biology and signal transduction. After obtaining PhD degree in Biochemistry from the Weizmann Institute of Science in Israel, he did two Post-doctorate trainings, first in the University of Texas Health Science Center in Dallas, USA and the second in the NIH, USA. He has then returned to Israel to the Weizmann Institute of Science and became Associate Professor in 1987. He has spent 1 year in the University of Kobe, Japan for a Sabbatical working with the late Y. Nishizuka (1988). Upon returning to Israel, he has joined the Department of Biochemistry at Tel Aviv University, Israel where he is currently working as a Professor.

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