ID-LctPR-40 – anti-hypoxia treatment of prostate hyperplasia and cancer

Cancer tissue hypoxia is one of the leading causes in the development of radiotherapy and chemotherapy resistance. In addition, it predisposes to the development of a tumour metastatic process. Prostate hyperplasia, although a benign tissue overgrowth, has also a hypoxic microenvironment.

There are only a few and indirect therapeutic approaches to target cancer hypoxia, and these are predominately limited to stimulating angiogenesis to improve vascularisation of the affected tissues.

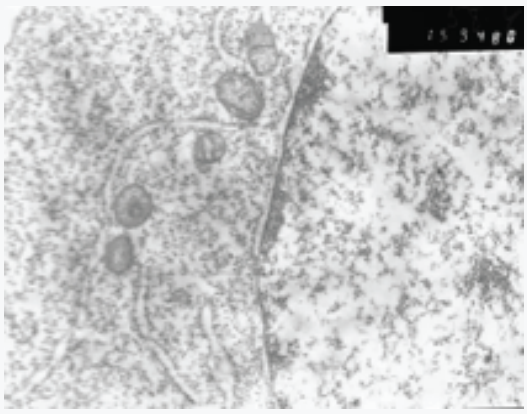
ID-LctPR-40 is the first pharmaceutical candidate developed to stimulate growth of the mitochondria and activate mitochondrial respiration and tissue oxygenation, targeting in particular the prostate.

ID-LctPR-40 is a composite product based on the combination of a prime molecule, *trans*-Lycopene, which has tropism to the prostate, and two chaperone molecules facilitating lycopene targeted delivery and its efficacy.

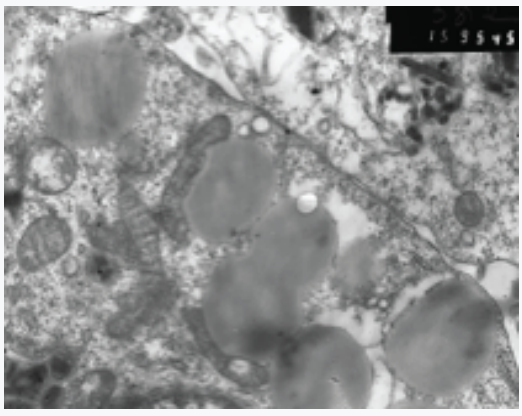
The Prime

trans-Lycopene is the prime molecule of ID-LctPR-40. In cell culture experiments this molecule has the ability to stimulate growth and respiration of the mitochondria, figure 1.

Fig. 1 Lycopene boosts growth and respiration of the mitochondria,
in vitro incubation with B10.MLM cells, transmission electron microscopy x 17,000



Control cells



+ *trans*-Lycopene

1st Chaperone - scaffolding

Since lycopene isomers are highly hydrophobic, they can be transported in the circulation only by lipoproteins. If their assembly, which predominately happens in enterocytes and the liver, is impaired, then the concentration of these molecules in the blood and in other organs will be reduced, therefore having poor bioavailability in middle-aged and older persons, and in those who have fatty liver or metabolic syndrome.

To overcome this problem, a chaperone molecule was added to the formulation in order to work as scaffolding to facilitate incorporation of the *trans*-Lycopene into newly assembling lipoproteins.

2nd Chaperone – chylomicron delivery

The liver and prostate are the two main organs with the highest level of carotenoid receptors. Therefore, to minimise delivery of lycopene to the liver, hence providing more opportunity for the absorbed lycopene to reach the prostate, it was necessary to explore a large chylomicron pathway. For this purpose it was necessary to introduce 2nd chaperone molecules, which would facilitate formation of large chylomicrons, which would go not to the portal vein and to the liver, but to the lymph system and then to the main circulation.

Pharmacokinetics

In pharmacokinetic clinical studies on middle-aged persons it was demonstrated that administration for 4 weeks of the ID-LctPR-40 formulation provided a significantly higher concentration of lycopene than when it was taken in its conventional form, not only in the circulating blood, but also in the cerumen, which may reflect its peripheral tissue build-up.

Pharmacodynamics

Higher bioavailability lycopene in this age cohort translated into a significantly higher level of molecular Oxygen transported by blood lipoproteins. In a randomised, double-blinded trial on 16 middle-aged persons, it was demonstrated that administration of lycopene in ID-LctPR-40 for 4 weeks, the period required to reach saturation level of the molecule in blood and tissues, resulted in an increase of the plasma O_2 by 4.3 + 0.5 μM. Administration of a conventional form of lycopene in the same dose, and for the same period, resulted in a significantly lower increase of this parameter, by 1.2 + 0.3 μM.

Clinical Trial Proof-of-concept

In a randomised, double-blinded clinical study, on 8 patients with moderate prostate hyperplasia (International Prostate Symptom Score (IPSS) > 16), it was demonstrated that administration of ID-LctPR-40 for 3 months resulted in an improvement of the IPSS by 12.3 + 2.2 points, whilst in the group which received lycopene in the same dose, but in a conventional form, the improvement of the score was only by 4.1 + 3.7.

Next Step

The main objective at the next step is to find funding and/or a partner to take ID-LctPR-40 to Phase II clinical trials for prostate hyperplasia and prostate cancer treatment. The anti-hypoxic activity of the product could be explored both as an adjuvant therapy for both radio- and chemotherapy to improve their efficacy, and also as an independent therapeutic product.

Regulatory

All molecules comprising GA-Lct-40 are safe for humans, and do not require FDA or other countries' regulatory body approval for oral administration in their therapeutic dose-range.

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