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Stem Cells in *In Vitro* Fertilisation (IVF): Hope or Hype?

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My dear friend, colleague and mentor Bob Edwards (who received the Nobel Prize for his work on *in vitro* fertilisation) (IVF) actually had a deep and profound interest in stem cell technology[1-3]. I was even lucky enough to be supervised by Bob Edwards for my PhD at Cambridge University on the stem cells found in the developing mouse embryo. IVF and stem cell technology, therefore, have a long history together which few people may realise. Despite this long joint history there has been little progress in the use of stem cell technology in IVF. This Editorial will briefly explore the past history of stem cells in IVF and then look at the future which is not only potentially exciting but also potentially ground-breaking.

Perhaps the most obvious link to IVF and stem cells is the development of human embryonic stem cells (hESC) from the inner cell mass of human embryos[4]. Whilst hESC are pluripotent and, therefore, an excellent candidate for gamete production, very little progress has been made because of the legal, ethical, moral and religious objections to creating hESC which requires the destruction of a viable human embryo[5]. More recently, it has been shown that mouse pluripotent mouse ESC can be reprogrammed into totipotent cells[6] which have been termed totipotent-like stem cells (TLSCs). It is possible that these TLSCs may give new insights into totipotency and embryology.

Induced Pluripotent Stem Cells (iPSCs) have a similar history when it comes to IVF. These are somatic cells (e.g. skin cells) which are 'transformed' into pluripotent stem cells by the introduction of various genes[7]. These iPSCs are pluripotent and autologous so they have the ability, in theory, to carry out gametogenesis[8] in patients undergoing fertility treatment. The problems with the routine clinical use of iPSCs in fertility treatment is the cost

but most importantly ongoing safety concerns about iPSCs because of the genes needed to be inserted to convert a somatic cell into a stem cell[9].

Mesenchymal stem cells (MSCs) can be obtained from adipose tissue, bone marrow, the umbilical cord and even inside teeth[10]. These MSCs can produce bone, connective tissue and adipose tissue and there are some data suggesting that MSCs may be useful in premature ovarian failure[11]. The drawbacks of using MSCs in the treatment of infertility are the cost and the standardisation of MSCs to ensure safety and efficacy[12]. All of these stem cell types have their problems when considering their use in the treatment of infertility. It may be many years, if ever, before they come to routine clinical practice in the treatment of infertility.

It has been shown that human Very Small Embryonic-Like (hVSEL) stem cells are found in every tissue of the body and in the peripheral blood[13]. They can easily be obtained from peripheral blood by preparing Platelet Rich Plasma (PRP) which has high numbers of hVSEL stem cells[14]. The hVSEL stem cells are pluripotent and arise from the primordial germ cell[15] making them the ideal stem cell to use in autologous format in the treatment of infertility[16]. Most workers agree that the hVSEL stem cells in the peripheral circulation are biologically inactive (quiescent)[17]. Despite this, we have shown that hVSEL stem cells in PRP made from peripheral blood can be biologically activated by a modulated laser (called the QiLaser). Following exposure of the QiLaser to hVSEL stem cells in PRP they become biologically active possibly through a mechanism of action involving quantum mechanics[14,18]. This means that in hVSEL stem cells

we have a source of biologically active pluripotent stem cells which can be easily collected from peripheral blood for autologous treatment[14]. This makes hVSEL stem cells an ideal candidate stem cell to treat both male and female infertility very easily and cheaply[19].

Further clinical trials are needed in order to fully assess the potential of autologous QiLaser activated hVSEL stem cells in PRP. Our unpublished data to date show significant benefits of simple intravenous infusion of QiLaser activated hVSEL stem cells not only in the treatment of infertility but also in the treatment of the menopause. These QiLaser activated hVSEL stem cell technologies hold great hope for a new generation of treatments for infertility, which may revolutionise the way in which we think about and treat this condition.

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