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The Real Captain America: Bioengineering the Super Soldiers of Tomorrow

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With the rapidly advancing field of genomics and gene modification, the distinct possibility has arisen for applying these technologies to enhance a soldier's physical capacity. Genetic modification or "gene doping", already banned from its possible future use in the Olympics, has many further applications that could enhance the operational performance of soldiers. Conceptual frameworks illuminate the "realm of the possible" which, if implemented, could in reality realize the much fabled concept of the "super soldier".

The World Anti-Doping Agency (WADA) defines gene doping as "the therapeutic use of genes, genetic elements, and/or cells that have the capacity to improve athletic performance". Thus, this technology, originally developed for treatment of disease, can be adapted to dramatically improve physical performance. Gene doping would use developments that manipulate DNA in the most basic regulation of biologic processes, thus increasing speed, power and endurance beyond what is achievable through natural diet and training (Gaffney, 2007). The leap from application in athletics to warfighting is a small one, and one that has the capacity to greatly enhance the performance of the individual soldier. With the increasing worldwide focus on developing more agile, smaller and lethal forces and the investment in Special Operations soldiers, focused applications to enhance the soldier at the individual level holds great appeal. The creation of super soldiers could be planned by well-placed genetic physiologic tweaks.

Methods of Manipulating Genes

Simply speaking, artificial genes can be introduced by direct injection of DNA into a muscle, insertion of genetically modified cells, and introduced into the body via a virus (Unal, 2004). An advantage unique to gene therapy is that by continuous production of the protein *in vivo*, the pharmacodynamic peaks and troughs of injected substances are eliminated, thus providing a steady delivery (Wells, 2008). For gene therapy, a vector is needed to transfer genetic material into cells. Viruses such as lentiviruses are slow acting and can introduce genes into a host genome. When modified, they are efficient delivery systems for gene therapy. The properties of the gene therapy to be delivered can be separated from the pathogenic consequences of the viral replication by removal of the disease causing genes. This space then can be filled with the therapeutic genes prior to introduction into the body (Wells, 2008).

Current science has illuminated several key areas to increase physical performance through gene doping. These include, endurance, strength, pain tolerance, improved energy levels and enhanced vascularity. Each of these areas have benefit to the warfighter.

Enhancing Endurance

Due to “blood doping” in international cycling, increasing endurance through hormone administration (not gene doping) is somewhat well known to the public. Erythopoetin (EPO) increases red blood cell (RBC) mass and oxygen delivery to muscles, thus greatly aiding in endurance related activities (Gaffney, 2007). However, using gene doping, EPO could be delivered to the soldier by viral vector and the subsequent increased oxygen carrying capacity of the blood would increase the overall endurance performance. This would be particularly useful for soldiers on patrol, on long-range reconnaissance, or participating in a long duration combat engagement. Physical fatigue is a well-known performance degradant that decreases readiness, and taken to an extreme, makes soldiers unable to complete the mission. The levels of EPO that could be delivered by gene-doping far exceeds the amount that would be developed naturally even in highly trained athletes. Furthermore, enhancement of the proteins known as hypoxia inducible factor (HIF), which modulate activity in low oxygen environments, would increase the production of red blood cell count and increase cellular energy (Gaffney, 2007). This particular gene tweak could be applied to soldiers operating in high elevation mountain warfare to possibly offset the adverse effects of altitude sickness.

In addition to increasing RBC for oxygen carrying purposes, expression of slow twitch muscle fibers for endurance focused activities could be modified via gene doping. Peroxisome proliferator-activated receptor delta (PPAR-delta), when expressed in activated form in skeletal muscle, increased the running endurance of transgenic mice to double that of their all natural counterparts (Wells, 2008). As such, gene transfer of PPAR-delta in soldiers may improve endurance capacity by increasing the proportion of oxidative slow twitch fibers.

Enhancing Strength

Physical strength is essential for the individual solider to carry out military related tasks and fight on the battlefield. It is even more important for special operations soldiers who may engage in close quarters battle and combatives. Gene doping affords a few different options to increase muscle size and strength. Growth hormone (GH) has possible anabolic effects on muscle proteins and connective tissue in human skeletal muscles. Recombinant GH is already being used as a doping agent in sports. Looking forward, insulin-like growth factor 1 (IGF-1) is a protein that stimulates cellular proliferation, somatic growth and differentiation. The skeletal specific IGF-1 has been observed to dramatically increase muscle hypertrophy in mice as well as reverse age-related muscle atrophy and aid muscle recovery (Wells, 2008). Gene transfer of IGF-1 into muscles using viral vectors could conceivably have a large impact on human muscle size and strength. Further strength enhancements could be made by tweaking myostatin. Myostatin is a protein that acts as a negative regulator of muscle mass –it “turns off” muscle growth. When the myostatin gene in mice has been inactivated, muscle hypertrophy was observed. Blockage of the myostatin action has the potential to allow soldiers to rapidly increase muscle mass. This blockade could be achieved at multiple levels such as increasing the expression of myostatin’s counterpoint, follistatin or by utilizing a humanized monoclonal antibody (Wells, 2008). In natural genetic modifications where myostatin is suppressed, as in the case of “Wendy the Whippet”, it produces superphysiologic muscle growth and reduces fat.

Improved Vascularity

Vascular endotheial growth factor has been shown to increase the production of new blood vessels in the case of peripheral arterial diseases. An increase in the production of new blood vessels would increase blood flow, oxygen and nutrients to the heart, liver, muscles and lungs and delay exhaustion (Unal, 2004). As with genetic improvements to endurance, improvements to vascularity would make the soldier’s body

more efficient and prolong the ability to fight or engage in other military tasks and thus increase combat effectiveness.

Increased Pain Tolerance

Introduction of genes producing analgesic endorphins and enkephalins would increase the pain threshold for the soldier. These genes would work equally well for both acute or chronic injury as well as lactic acid build up as a result of continuous physical effort (Gaffney, 2007). These natural narcotic peptides could replace the need for both anti-inflammatory and anti-pain medication, subsequently reducing the need to carry these type of supplies on the mission while providing a solution to alleviating physical discomfort and pain.

Increasing Energy

Enhancing the metabolic efficiency and performance of a soldier would also increase readiness and increase combat performance. Adenosine triphosphate (ATP) is the immediate source of energy for all cellular processes. The two major sources for ATP are the tricarboxylic cycle and the electron transport chain and glycolysis. Mitochondria produce roughly 80 percent of a cell's energy and millions of years of evolution has produced highly efficient pathways with similar structural features. However, there is no generic mitochondrion and the cell, tissue-specific and individual differences remain to be studied and exploited (Valdes, 2010). By utilizing metabolomics, a "snapshot" could be taken of a soldier's individual blood chemistry. This snapshot could then serve as a baseline to tailor individual performance enhancing elements such as diet and training. Looking towards genetic engineering, however, more opportunities exist. Metabolic engineering, the directed improvement of cellular processes through the modification of specific biochemical reactions or the introduction of new ones, will allow for the increase of ATP synthesis. Genetic manipulation of the ADP transporter has the potential to increase its efficiency, thus making more ADP available for phosphorylation to ATP (Valdes, 2010). In addition, increasing respiratory chain supercomplexes known as respirasomes via genetic engineering could result in increasing ATP production. This is the area with greatest potential to enhance metabolic efficiency (Valdes, 2010).

Conclusion

A variety of genetic engineering or "gene doping" methods exist that could greatly enhance the performance of the soldier. By providing capabilities beyond what can be naturally developed through diet and training, gene manipulation has the potential to create stronger, faster, more energetic and pain resistant super soldiers. Although the science is still developing for gene therapy purposes, these types of capabilities are within the realm of the possible. In addition, the safety factor of genetic manipulation still needs improvement. Various gene therapy testing approaches on animals has resulted in a variety of negative health effects to include death. Living in the age of biotechnology, personal performance and health improvements via genetic manipulation is inevitable and the applications to increase the warfighting capacity of the soldier are apparent.

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