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Don't market stem-cell products ahead of proof

The controversy over an unproven stem-cell therapy in Italy highlights the dangers of doing translational medicine in reverse, argues **Paolo Bianco**.

Translational medicine is said to reflect a need to harness the huge wealth of scientific knowledge in biomedicine. In fact, it is a direct consequence of the globalized outsourcing of research and development by the pharmaceutical industry, resting on the creation of commercial enterprises within academia. A commercial drive in academia can, however, significantly alter scientific concepts in biology and medicine.

Mesenchymal stem cells (MSCs) provide a prime example of this. Decades of research on these cells, found in the bone marrow, show that they go on to form skeletal tissues such as bone, fat and cartilage, which they can also help to regrow and repair in the clinic. Yet companies have already emerged that market MSCs for a much broader range of applications. Against mainstream scientific evidence, these firms argue that the cells are veritable injectable drug stores.

This commercial creep has reached the pages of authoritative scientific journals, with articles suggesting that intravenously infused MSCs can be used as a single agent to mute or cure a long list of unrelated diseases in multiple organs, regardless of their cause and nature. Notably, these include terminal neurodegenerative diseases, strokes and heart attacks. These are extraordinary claims that would require extraordinary evidence, which, in my view, does not yet exist. The very concept of MSCs has become divorced from that of a stem cell found in bone marrow. The scientific literature now contains two conflicting descriptions of these cells — one based on science, another on commerce.

Industry has not yet generated conclusively proven medicinal products or major novel technologies to better harness the biology of MSCs. However, commercial interest has profoundly influenced the definition of these cells (and of their clinical potential) within the scientific community. This is translational medicine in reverse. Commercial products have been converted into scientific concepts. It highlights an important dark side of the commercialization of science.

The marketing of MSCs as a cure-all is no coincidence — they have long been credited with potential performances that are beyond their biological limits. A decade or so ago, they were promoted as an ethical alternative to pluripotent stem cells derived from human embryos. They lost that unique selling point with the arrival of a technique to genetically reprogram adult cells into pluripotent cells. Suddenly, MSCs became 'pluri-effective' through intravenous infusions and release of chemical factors. Yet intravenously infused MSCs die rapidly and are quickly cleared from the body. As shown by 50 years of *in vivo* experiments, locally transplanted MSCs form bone. They do so, data show, even if transplanted into the heart or brain.

How MSCs would mute or cure unrelated diseases has never been fully explained, in my view. Proponents say that the cells would restore brain function by nurturing cells with chemical factors. This remains unproven. With no reliable preclinical rationale, trials of MSCs can never be anything other than inconclusive. The only winners are the firms wishing to sell the therapies, which add the trial details — if not the results — to their marketing brochures.

Some 300 clinical trials on MSC infusions have been, or are being, conducted worldwide. Their mere initiation, paradoxically, is used to suggest that intravenously infused MSCs can cure multiple unrelated diseases, which (to my knowledge) is not proven at this time. These statements, and the trials that fuel them, represent a new kind of advertisement within science. They can distort science and medicine, mislead the public, create illusions for patients, sabotage health-care systems and, above all, obstruct rather than accelerate the growth of science and the development of medicine from it.

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This is a worldwide problem, highlighted by current events in Italy. A Brescia-based organization called the Stamina Foundation is promoting an unproven MSC therapy to vulnerable patients, including children with lethal neurological diseases. This has in effect forced the Italian government to test the therapy in a government-funded clinical trial, to cope with a media-generated social crisis and the risk of infringing European regulations on stem-cell therapies. Last week, *Nature* called for the trial to be scrapped (see *Nature* **499,** 125; 2013) as evidence emerged of terminal flaws in the biology behind the purported cure. Stamina is backed by companies and a lobbying organization called the Cure Alliance, which has offices in Milan and Rome.

Central to the agenda of those who promote unproven therapies is an attack on the regulations surrounding such treatments, as well as the regulatory bodies that enforce them. Bone-marrow transplantation, some say, would never have been developed under today's stringent regulations. But bone-marrow transplantation was never a commercial product, and it developed when no one was out to sell stem cells directly to patients and ahead of proof.

Translating science into effective medicine cannot be based on indiscriminate development of commercial products. The push to fund commercial science and the seep of commercial descriptions of natural objects within academia can severely affect science, medicine and the economy. Claiming the right to market products ahead of proof of efficacy can only bring ineffective products to market, degrade medicine and impoverish all except, perhaps, the fortunate sellers. ■

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