Stem Cells in Orthopedics, Current Concepts and Possible Applications

Essay

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BY
Marco Shawky Wanees
M.B.B.CH
Ain Shams University
Supervised by

DR/ Abdelfattah Mohamed fathy Saoud
Associate Professor of Orthopedic Surgery
Faculty of Medicine
Ain Shams University

DR/Magdy Saad Mahmoud
Lecturer of Orthopedic Surgery
Faculty of Medicine
Ain Shams University

Faculty of medicine

Ain Shams University

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Introduction

A stem cell is a cell that has the ability to divide for indefinite periods - often through out the life of an organism. The stem cells, when provided with the right signals, have the potential to differentiate into different types of cells that constitute an organism. These cells when differentiated can have a characteristic shape and specialized functions, such as heart cells, skin cells or nerve cells. In short, stem cells have two distinctive properties, one they can make identical copies of themselves for a long period of time (self renewal) and two give rise to mature cells that have a characteristic morphology, function [1].

Typically stem cell generates an intermediate cell type or different cell types prior to achieving a mature differentiated state. The intermediate cell is called a precursor or progenitor cell [1, 2].

Precursor or progenitor cells in fetus or adults are partially differentiated cells and eventually divide and give rise to mature differentiated cells. These cells tend to differentiate only along a particular cellular development pathway; however, some recent studies have shown that this may not be as definitive as was once thought [1, 2].

Their use in orthopedics has gained a significant momentum in past few years and researches done on their use in various orthopedic subspecialties [3].

Some issues remain at the forefront of the controversy involving stem cell research legislation, ethics and public opinion, cost and concentration methods .Legislations regarding the use of stem cells vary among different countries as does the public opinion and the moral high grounds assumed by various political and religious groups

Researchers argue that many of the embryos created by in vitro fertilization programs are surplus to requirements and are in any case normally destroyed thus they use them as a source of stem cells [3].

Costs involved in stem cell research are astronomical and thus is limited to centers that can invest huge sums of money for various projects. This cost is eventually passed to patients and the health care system. With time however it is expected that cost would bottom down and the technology may be affordable to most candidate patients [3].

One of the challenges that clinicians face while using the adult stem cell is that of concentrating the cells. The normal concentration of stem cells in samples drawn from marrow is considered inadequate for use in most scenarios. Various techniques like filtration and culture expansion are employed for this purpose [3].

Success of stem cells in various modalities has been limited by problems of dosage, lack of activity of the recombinant factor and the inability to sustain the presence of a factor for an appropriate length of time. Also the risk of forming unwanted tissues and teratocarcinoma by the stem cells requires further evaluation and long term follow up [4].

The use of stem cell in orthopedics has provided a new arena for managing complex conditions. Its use holds promise of wide spread applications particularly in areas of spinal cord injury, difficult non- unions, cartilage repair and degenerative disc disorders [4].

However, its use at present times is restricted by lacunas in our knowledge in differentiating potentials of these cells and concerns over the long term stability of repair tissue derived from these cells. In view of concerns rose by certain politico-religious groups and also as with any new technology, the enthusiasm for this technology that has potential to influence virtually every orthopedic case management must be balanced by subjecting it to clinical and basic research investigations[4].

Aim of the study

This study aims at stressing on the stem cell basics; biology which provided a new arena for managing complex conditions. With special emphasis on its uses in orthopedics whish holds promise of wide spread applications particularly in areas of spinal cord injury, difficult non- unions, cartilage repair and degenerative disc disorders

References

1. Harley CB, Gearhart J,Jaenisch R,Rossant J,Thomson J. Pluripotent stem cells: Biology and applications. Durango Publisher Co: 2001.
2. Caplan AI. Review: mesenchymal stem cells: Cell-based reconstructive therapy in orthopedics. Tissue Eng 2005.
3. Vats A, Tolley NS, Buttery LD, Polak JM. The stem cell in orthopedic surgery. J Bone Joint Surg Br.2004; 86:159-64.
4. Pittenger MF, Marshak DR. Mesenchymal stem cells of human adult bone marrow. Marshak DR, Gardner DK and Gottlieb D. editors. Cold Spring Harbor Laboratory Press. Cold Spring Harbor: New York; 2001. p. 349-74.
5. Buttery LD, Bourne S, Xynos JD, Wood H, Hughes FJ, Hughes SP, et al . Differentiation of osteoblasts and in vitro bone formation from murine embryonic stem cells. Tissue Eng 2001; 7:89-99.
6. Bruder SP, Jaiswal N, Haynesworth SE. Growth kinetics, self-renewal and the osteogenic potential of purified human mesenchymal stem cells during extensive subcultivation and following cryopreservation. J Cell Biochem 1997; 64:278-94.
7. Pereira RF, Halford KW, O'Hara MD, Leeper DB, Sokolov BP, Pollard MD, *et al* . Cultured adherent cells from marrow can serve as long-lasting precursor cells for bone, cartilage and

lung in irradiated mice. Proc Natl Acad Sci USA 1995; 92:4857-61.

8. Solchaga LA, Welter JF, Lennon DP, Caplan AI. Generation of pluripotent stem cells and their differentiation to the chondrocytic phenotype. Methods Mol Med 2004; 100:53-68.
9. Kuangshin Tai, Gadi Pelled, Dima Sheyn, Anna Bershteyn, Lin Han, Ilan Kallai, Yoram Zilberman, Christine Ortiz and Dan Gazit. Nanobiomechanics of Repair Bone Regenerated by Genetically Modified Mesenchymal Stem Cells. Tissue Engineering: 2008
10. Enrico Lucarelli, Davide Donati, Annarita Cenacchi, Pier Maria Fornasari. Bone reconstruction of large defects using bone marrow derived autologous stem cells. Transfusion and Apheresis Science 30 (2004) 169–174
11. Okano H, Okada S, Nakamura M, Toyama Y. Neural stem cells and regeneration of injured spinal cord. Kidney Int 2005; 68:1927-31.
12. Magne D, Vinatier C, Julien M, Weiss P, Guicheux J. Mesenchymal stem cell therapy to rebuild cartilage. Trends Mol Med. 2005; 11:519-26.
13. Murphy JM, Fink DJ, Hunziker EB, Barry FP. Stem cell therapy in a caprine model of osteoarthritis. Arthritis Rheum 2003; 48:3464-74.
14. Lim JK, Hui J, Li L, Thambyah A, Goh J, Lee EH. Enhancement of tendon graft osteointegration using

mesenchymal stem cells in a rabbit model of anterior cruciate ligament reconstruction. Arthroscopy 2004;

15. Hasharoni A, Zilberman Y, Turgeman G, Helm GA, Liebergall M, Gazit D. Murine spinal fusion induced by engineered mesenchymal stem cells that conditionally express bone morphogenetic protein-2. J Neurosurg Spine 2005; 3:47-52.
16. Risbud MV, Shapiro IM, Guttapalli A, Di Martino A, Danielson KG, Beiner JM, *et al* . Osteogenic potential of adult human stem cells of the lumbar vertebral body and the iliac crest. Spine 2006; 31:83-9.
17. Cinotti G, Patti AM, Vulcano A, Della RC, Polveroni G, Giannicola G, *et al* . Experimental posterolateral spinal fusion with porous ceramics and mesenchymal stem cells. J Bone Joint Surg Br 2004;86:135-42
18. Risbud MV, Shapiro IM, Vaccaro AR, Albert TJ. Stem cell regeneration of the nucleus pulposus. Spine J 2004;
19. Acosta FL Jr, Lotz J, Ames CP. The potential role of mesenchymal stem cell therapy for intervertebral disc degeneration: A critical overview. Neurosurg Focus 2005;
20. Sakai D, Mochida J, Iwashina T, Watanabe T, Nakai T, Ando K, et al. Differentiation of mesenchymal stem cells transplanted to a rabbit degenerative disc model: potential and limitations for stem cell therapy in disc regeneration. Spine 2005;30:2379-87

21. Sakai D, Mochida J, Iwashina T, Hiyama A, Omi H, Imai M, *et al* . Regenerative effects of transplanting mesenchymal stem cells embedded in atelocollagen to the degenerated intervertebral disc. Biomaterials 2006; 27:335-45.
22. Kristina Hug. Sources of human embryos for stem cell research: ethical problems and their possible solutions. Medicina (Kaunas) 2005; 41(12)
23. Louis M. Solomon and Sandra A. Brockman-Lee. Embryonic Stem Cells in Science and Medicine, Part II: Law, Ethics, and the Continuing Need for Dialogue. Gender medicine/vol. 5, NO. 1, 2008

المقدمة

الخلايا الجذعيه هي الخلايا التي لها القدرة على الانقسام لفترات غير محدودة خلال حياة الكائن حي.

الخلايا الجذعيه ، عند قدوم الإشارات الصحيحة ، لديها القدرة على التحول إلى أنواع مختلفة من الخلايا التي تشكل كائن حي. هذه الخلايا عندما تتحول يمكن ان يكون لها خاصية الشكل والوظائف المتخصصة مثل خلايا القلب ، وخلايا الجلد أو الخلايا العصبية.

باختصار ، الخلايا الجذعيه لها اثنين من الخصائص المميزة ، الأولى هي أنها يمكن ان تنقسم إلى نسخ متطابقة من نفسها لفترة طويلة من الزمن (تجديد الذات) ، والثانية هي ان تعطى الخلايا الناضجة التي لها خاصية الشكل والوظائف المتخصصة .

وعادة ما تولد الخلايا الجذعيه الخلية الوسيط أو اى نوع مختلف من أنواع الخلايا قبل تحقيق الأنسجة الناضجة المتباينة . الخلية الوسيط تسمى خلية السلف .

الخلايا الجذعية في خلايا البالغين متباينة وتنقسم الخلايا وتؤدي إلى خلية ناضجة متباينة هذه الخلايا غالبا تميل إلى التميز على طول طريق النمو الخلوي .

استخدامها في جراحة العظام اكتسب أهمية كبيرة في السنوات القليلة الماضية والكثير من البحوث قدمت في الوقت الحاضر.

هذا البحث يقدم المفهوم الحالي وبعض التطبيقات الممكنة في المستقبل للخلايا الجذعية في جراحة العظام وهى مثلا :

تجديد النخاع الشوكى ، عدم التئام العظام ، إصلاح الغضروف ، علاج انحلال أقراص الغضروف بين الفقرات

التحديات والطريق إلى الأمام :

بعض المسائل لا تزال في طليعة الجدل على بحوث الخلايا الجذعيه القوانين والأخلاق والرأي العام ، من حيث التكلفة و التشريعات فيما يتعلق باستخدام الخلايا الجذعيه تتفاوت فيما بين البلدان المختلفة وكذلك الرأي العام .

ويرى الباحثون إن العديد من الاجنه التي أوجدتها برامج التخصيب في المختبر هي الفاءضه عن الحاجة وعلى أية حال هي تدمر طبيعيا. .

تكاليف المشاركة في بحوث الخلايا الجذعيه فلكيه ، وبالتالي يقتصر على المراكز التي يمكن ان تستثمر مبالغ ضخمة من المال لمشاريع مختلفة. هذه التكلفة في نهاية الأمر يتم نقلها إلى المرضى ونظام الرعاية الصحية. ولكن مع مرور الزمن من المتوقع ان تقل التكلفة والتكنولوجيا قد تكون في متناول معظم المرضى .

واحدا من التحديات التي تواجه الأطباء في استخدام الخلايا الجذعيه البالغة هى تركيز الخلايا. التركيز الطبيعي للخلايا الجذعيه في عينات من النخاع هو في كثير من الأحيان غير كافي لاستخدامها في معظم الأبحاث .

نجاح الخلايا الجذعيه في مختلف الطرق المتعلقة كان محدودا بسبب مشاكل الجرعة و أيضا من خطر تكوين الانسجه غير المرغوب فيها ، الخلايا الجذعيه تحتاج إلى مزيد من التقييم والمتابعة على المدى الطويل .

الخلايا الجذعيه في جراحة العظام ،
المفهوم الحالي والتطبيقات الممكنة

بروتوكول رسالة

مقدمة من

طبيب / ماركو شوقى ونيس

توطئة للحصول علي درجة الماجستير في جراحة العظام

تحت إشراف

د / عبد الفتاح محمد فتحى سعود

أستاذ مساعد جراحة العظام

كلية الطب–جامعة عين شمس

د / مجدى سعد محمود

مدرس جراحة العظام

كلية الطب–جامعة عين شمس

كلية الطب

جامعة عين شمس

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