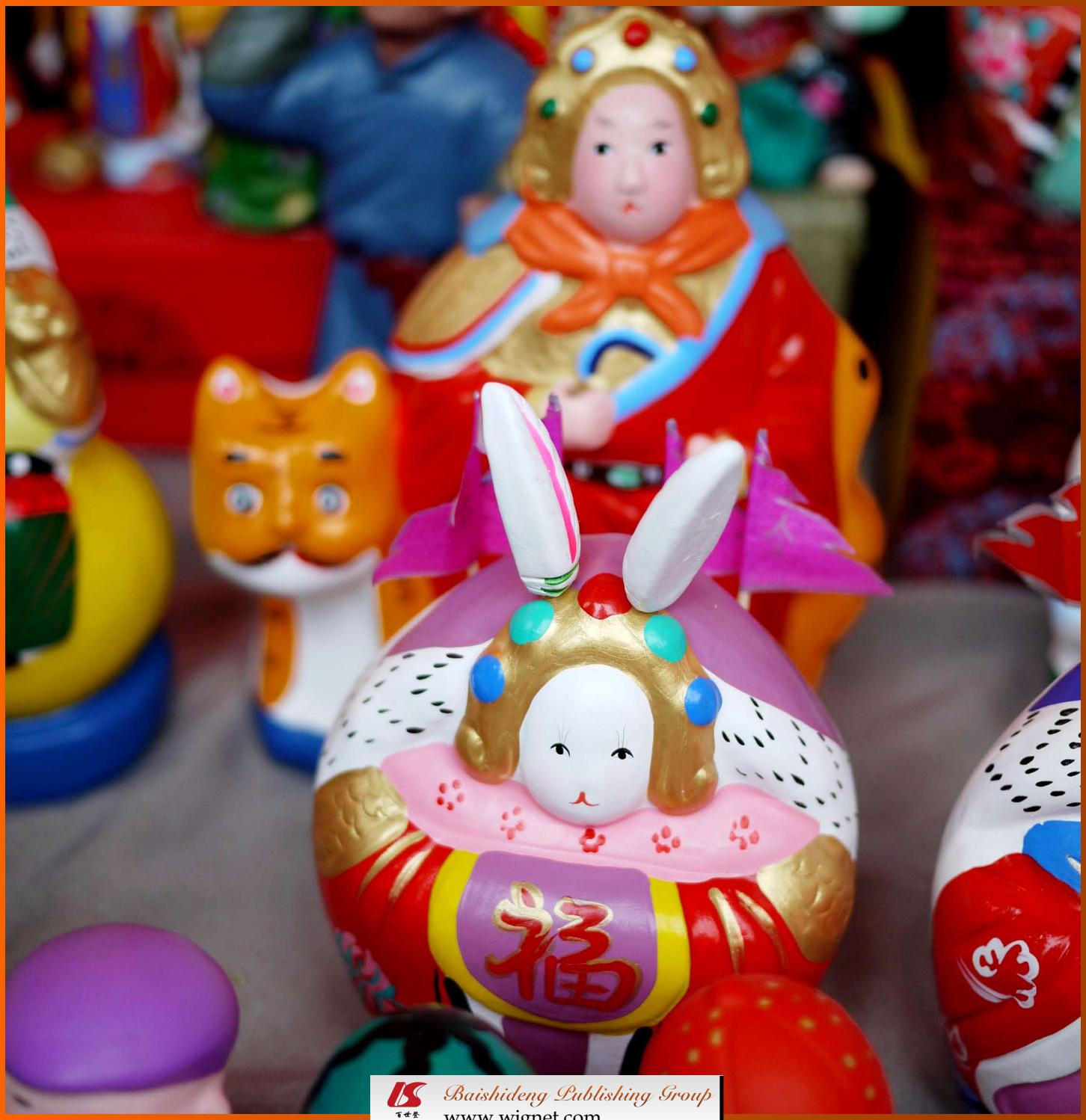
ISSN 1948-0210 (online)

World Journal of *Stem Cells*

World J Stem Cells 2011 March 26; 3(3): 19-24



Baishideng Publishing Group
www.wjgnet.com

WJSC World Journal of Stem Cells

A peer-reviewed, online, open-access journal of stem cells

Editorial Board

2009-2013

The *World Journal of Stem Cells* Editorial Board consists of 284 members, representing a team of worldwide experts in stem cells research. They are from 28 countries, including Australia (5), Austria (1), Belgium (3), Brazil (2), Canada (7), China (19), Czech Republic (2), Denmark (4), Finland (3), France (5), Germany (14), Hungary (3), India (3), Iran (1), Israel (4), Italy (13), Japan (18), Netherlands (4), Norway (2), Singapore (10), South Korea (15), Spain (6), Sweden (2), Switzerland (3), Turkey (2), United Arab Emirates (1), United Kingdom (15), and United States (117).

WJSC

World Journal of Stem Cells

Contents

Monthly Volume 3 Number 3 March 26, 2011

World Journal of Stem Cells
Volume 3 Number 3 March 26, 2011

Contents

NAME OF JOURNAL
World Journal of Stem Cells

LAUNCH DATE
December 31, 2009

SPONSOR
Beijing Baishideng BioMed Scientific Co., Ltd.,
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: 0086-10-8538-1892
Fax: 0086-10-8538-1893
E-mail: baishideng@wjgnet.com
http://www.wjgnet.com

EDITING
Editorial Board of *World Journal of Stem Cells,*
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: +0086-10-8538-1891
Fax: +0086-10-8538-1893
E-mail: wjsc@wjgnet.com
http://www.wjgnet.com

PUBLISHING
Baishideng Publishing Group Co., Limited,
Room 1701, 17/F, Henan Bulding,
No.90 Jaffe Road, Wanchai,
Hong Kong, China
Fax: 00852-3115-8812
Telephone: 00852-5804-2046
E-mail: baishideng@wjgnet.com
http://www.wjgnet.com

SUBSCRIPTION
Beijing Baishideng BioMed Scientific Co., Ltd.,
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: 0086-10-8538-1892
Fax: 0086-10-8538-1893
E-mail: baishideng@wjgnet.com
http://www.wjgnet.com

ONLINE SUBSCRIPTION
One-Year Price 108.00 USD

PUBLICATION DATE
March 26, 2011

SERIAL PUBLICATION NUMBER
ISSN 1948-0210 (online)

EDITORIAL OFFICE
Jin-Lei Wang, Director
World Journal of Stem Cells
Room 903, Building D, Ocean International Center,
No. 62 Dongsihuan Zhonglu, Chaoyang District,
Beijing 100025, China
Telephone: 0086-10-8538-1891
Fax: 0086-10-8538-1893
E-mail: wjsc@wjgnet.com
http://www.wjgnet.com

INSTRUCTIONS TO AUTHORS
Full instructions are available online at http://www.wjgnet.com/1948-0210/g_info_20100313165700.htm. If you do not have web access please contact the editorial office.

ONLINE SUBMISSION
http://www.wjgnet.com/1948-0210office

World Journal of Stem Cells

Online Submissions: http://www.wjgnet.com/1948-0210office
wjsc@wjgnet.com
doi:10.4252/wjsc.v3.i3.19

World J Stem Cells 2011 March 26; 3(3): 19-24
ISSN 1948-0210 (online)

EDITORIAL

Functional ion channels in stem cells

Gui-Rong Li, Xiu-Ling Deng

Gui-Rong Li, Departments of Medicine and Physiology, Li Ka Shing Faculty of Medicine, the University of Hong Kong, Pokfulam, Hong Kong, China
Xiu-Ling Deng, Department of Physiology and Pathophysiology, School of Medicine, Xi'an Jiaotong University, Xi'an 710049, Shaanxi Province, China
Author contributions: Li GR and Deng XL both contributed to this paper.
Supported by (in part) Grants (734703M and 8CRF09) from the Research Grant Council of Hong Kong, China
Correspondence to: Dr. Gui-Rong Li, Associate Professor, L4-59, Laboratory Block, FBM, Li Ka Shing Faculty of Medicine, The University of Hong Kong, 21 Sassoon Road, Pokfulam, Hong Kong, China. grli@hkucc.hku.hk
Telephone: +852-2819-9513 Fax: +852-2855-9730
Received: October 30, 2010 Revised: January 14, 2011
Accepted: January 21, 2011
Published online: March 26, 2011

Abstract

Bioelectrical signals generated by ion channels play crucial roles in excitation genesis and impulse conduction in excitable cells as well as in cell proliferation, migration and apoptosis in proliferative cells. Recent studies have demonstrated that multiple ion channels are heterogeneously present in different stem cells; however, patterns and phenotypes of ion channels are species- and/or origin-dependent. This editorial review focuses on the recent findings related to the expression of functional ion channels and the roles of these channels in regulation of cell proliferation in stem cells. Additional effort is required in the future to clarify the ion channel expression in different types of stem cells; special attention should be paid to the relationship between ion channels and stem cell proliferation, migration and differentiation.

Key words: Stem cells; Ion channels; Proliferation

Peer reviewer: Umberto Galderisi, PhD, Associate Professor, Department of Experimental Medicine, Second University of Naples, Via L. De Crecchio 7, 80138 Napoli, Italy

Li GR, Deng XL. Functional ion channels in stem cells. *World J Stem Cells* 2011; 3(3): 19-24 Available from: URL: http://www.wjgnet.com/1948-0210/full/v3/i3/19.htm DOI: http://dx.doi.org/10.4252/wjsc.v3.i3.19

STEM CELLS

Stem cells are found in all multi-cellular organisms and are characterized by the ability to self-renew through mitotic cell division and differentiate into a diverse range of specialized cell types. There are two types of original mammalian stem cells: embryonic stem cells and adult stem cells found in adult tissues. In addition, it has recently been found that induced pluripotent stem cells (iPS) can be developed from other types of cells including fibroblasts[1].

Embryonic stem (ES) cells are derived from mammalian embryos in the blastocyst phase of development[2,3]. Adult (or somatic) stem cells were initially isolated from mouse bone marrow[4]; further studies have shown that stem cells are present in different types of tissue including brain, heart, blood vessels, skeletal muscles, skin, liver and fat tissue. Adult stem cells remain in a quiescent or non-dividing state and can be activated by disease or tissue injury. In adults, stem cells/progenitor cells act as a repair system for the body and maintain the normal turnover of regenerative organs such as blood, skin and intestinal tissues[5].

iPS cells are recently developed cells induced from somatic cells such as skin fibroblasts and B lymphocytes[6]. They were generated initially by Takahashi & Yamanaka[1] by reprogramming somatic cells by over-expressing a combination of four transcription factors: octamer 3/4 (Oct4), SRY box-containing gene 2 (Sox2), Kruppel-like factor 4 (Klf4) and c-Myc in murine fibroblasts to induce the cells enter an embryonic-like state[1,7]. The iPS cells are then produced by introducing the four transcription factor–encoding genes into human fibroblasts[7]. Two other groups produced similar iPS cells by introducing slightly different combinations of genes: POU5F1 (OCT4), SOX2, NANOG and LIN28A (LIN28)[8,9]. These iPS cells are similar to ES cells in morphology, growth properties and expression of phenotypic markers. These cells closely

resemble ES cells and can differentiate into multiple types of cells *in vitro* and *in vivo*[1,6,7,9]. ES cells, adult tissue mesenchymal stem cells (MSCs) and their progenitors and iPS cells all possess potential therapeutic value in regenerative medicine.

In addition to the three major types of stem cells mentioned above that possess potential benefit for regenerative medicine, another type of stem cells is found within tumors or hematological cancers and has characteristics associated with normal stem cells, specifically the ability to give rise to all cell types found in a particular cancer sample. Cancer stem cells are tumorigenic in contrast to other non-tumorigenic cells[9] and may induce tumors through the stem cell processes: self-renewal and differentiation into multiple cell types. Moreover, cancer stem cells are believed to persist in tumors as a distinct population and cause relapse and metastasis by giving rise to new tumors. Therefore, cancer stem cells may be a target for developing specific therapies to improve survival and quality of life of cancer patients, especially sufferers of metastatic disease[10].

Although stem cells are important in regenerative medicine and/or cancer treatment, their cellular physiology and biology are not fully understood. Membrane ion channels are known to play a crucial role in proliferation, apoptosis and migration in a wide range of cells.

ION CHANNELS IN STEM CELLS

Multiple functional ion channel currents have been reported to be heterogeneously present in different types of stem cells. They include the voltage-gated delayed rectifier K^+ current I_{KDR} (encoded by different Kv genes), the Ca^{2+}-activated K^+ current K_{Ca} (including BK_{Ca}, large conductance K_{Ca}; IK_{Ca}, intermediate conductance K_{Ca}; and SK_{Ca}, small conductance K_{Ca}), the transient outward K^+ current I_{to} (or A-type current, I_A), inward rectifier K^+ current (I_{Kir}), hyperpolarization-activated cyclic nucleotide-regulated cation current (I_h), chloride current (I_{Cl}), voltage-gated Na^+ current (I_{Na}), L-type calcium current ($I_{Ca.L}$), transient receptor potential (TRP) nonselective cation currents. These currents have been found to be heterogeneously present in ES cells, mesenchymal stem cells (MSCs) from bone marrow, fat tissue and human umbilical cord vein, neural progenitor cells, cardiac progenitor cells or iPS cells derived from different species.

ION CHANNELS IN EMBRYONIC STEM CELLS

In ES cells, it has been reported that a tetraethylammonium (TEA)- and 4-aminopyridine (4-AP)-sensitive IK_{DR} is co-present with iberiotoxin-sensitive BK_{Ca} in 52% of mouse ES cells and homogenously present in (100%) human ES cells[11]. However, phenotypes of IK_{DR} differ between mouse and human ES cells. IK_{DR} is encoded by Kv1.1, Kv1.2, Kv1.3 and Kv1.6 genes in mouse ES cells and by Kv7.2 and Kv9.3 in human ES cells. Interestingly, a Cs^+-sensitive hyperpolarization-activated current (I_h, encoded by HCN3) is present in 23% of mouse ES cells but not in human ES cells. In addition, iberiotoxin-sensitive BK_{Ca} is encoded by MaxiK (Slo or KCa1.1) in mouse ES cells[11]. Although human ES cell and mouse ES cells share similar expression of many surface markers and intracellular signal pathways[12,13], significant differences are found in the expression of vimentin, h-III tubulin, alpha-fetoprotein, eomesodermin, HEB, ARNT and FoxD3 as well as in the expression of the LIF receptor complex LIFR/IL6ST (gp130)[12,14]. The different patterns and phenotypes of ion channel expression in human ES cells and mouse ES cells support the notion that some basic information on human ES cells can be derived from mouse ES cells; however, such information does not correspond on a one-to-one basis[14].

ION CHANNELS IN MESENCHYMAL STEM CELLS

A noise-like iberiotoxin-sensitive K_{Ca} and a 4-AP- and TEA-sensitive IK_{DR} are detected in most human bone marrow-derived MSCs[15,16]. The noise-like K_{Ca} is encoded by MaxiK (KCa1.1 or Slo) as demonstrated by several research groups[15-17]. Our study demonstrates that IK_{DR} shares similar characteristics with EAG channels cloned from the brain[18] which is encoded by hEAG1 (Kv10.1) in human MSCs[16]. In addition, a voltage-gated tetrodotoxin (TTX)-sensitive Na^+ current ($I_{Na.TTX}$, encoded by hNE-Na or Nav1.7), a 4-AP-sensitive I_{to} (I_A, encoded by Kv1.4 and Kv4.2)[16] and a nifedipine-sensitive $I_{Ca.L}$ (encoded by CACNA1C or Cav1.2) are present in a small population (29%, 8% and 15% respectively) of human MSCs[16].

IK_{Ca} current (encoded by KCa3.1 or KCNN4), volume-sensitive Cl^- current ($I_{Cl.vol}$, encoded by Clcn3) and I_{Kir} (encoded by Kir2.1) but not IK_{DR}, are present in mouse bone marrow-derived MSCs[19]. The patterns and phenotypes of ion channels in mouse MSCs are different from mouse ES cells, suggesting that ion channel expression is origin-dependent.

In addition to $I_{Na.TTX}$ (encoded by SCN2A), I_{to} (encoded by Kv1.4) and $I_{Ca.L}$ (encoded by CCHL2a) recorded in a small population (16%, 10% and 8% respectively) of rat bone marrow MSCs, 4-AP sensitive IK_{DR} (encoded by Kv1.2 and Kv2.1) is present in 91% of cells. BK_{Ca} (KCa1.1) and IK_{Ca} (KCa3.1) are co-present in 33% of rat MSCs[20]. Interestingly, IK_{DR} (encoded by Kv1.2 and Kv2.1) is present in 78% of rabbit bone marrow MSCs, BK_{Ca} and IK_{Ca} are co-expressed with IK_{DR} in 29% of cells, while I_{Kir} (encoded by Kir1.1) is present in 28% of cells[21]. These results demonstrate the different patterns and phenotypes of ion channels heterogeneously expressed in MSCs from mouse, rat, rabbit and human bone marrow, indicating a species-dependence of ion channel expression in bone marrow MSCs.

Interestingly, BK_{Ca}, $I_{Na.TTX}$, and I_{to} are present in 92%, 30% and 50% of MSCs from human umbilical cord vein and encoded by KCa1.1, hNE-Na, and Kv1.4 and Kv4.2 respectively[22], and Ba^{2+}-sensitive I_{Kir} (encoded by TWIK and Kir2.1) is present in 5% of cells. However, no typical IK_{DR} is recorded, although Kv1.1 and hEAG1 (Kv10.1)

genes are detected in these cells[22]. In MSCs from human fat tissue[23], $I_{Na.TTX}$ (encoded by hNE-Na) and 4-AP sensitive I_{to} are recorded in a small population (8% and 19%) of cells. In addition to 4-AP- and TEA-sensitive IK_{DR} (likely encoded by the multiple genes Kv1.1, Kv1.5, Kv2.1, Kv7.3, Kv11.1 and Kv10.1) recorded in 73% of cells, three types of K_{Ca} currents sensitive to inhibition by the BK_{Ca} blocker iberiotoxin, IK_{Ca} blocker clotrimazole and SK_{Ca} blocker apamin are present and the corresponding channel genes (KCa1.1, KCa3.1 and KCa2.3) are detected in human fat tissue-derived MSCs[23]. These studies suggest that patterns and phenotypes of ion channel expression in MSCs are species- and/or tissue-specific dependent.

ION CHANNELS IN NEURAL STEM/PROGENITOR CELLS

In neural stem/progenitor cells, an earlier study reported that two types of K^+ currents, IK_{DR} (encoded by Kv1.2, Kv1.5 and Kv1.6) and I_A (encoded by Kv1.4), were co-expressed in oligodendrocyte progenitor cells and differentiated cultured oligodendrocytes from neonatal rats[24]. Recent studies demonstrated that both Ba^{2+}-sensitive I_{Kir} (encoded by Kir4.1 and Kir5.1) and TEA-sensitive IK_{DR} (encoded by Kv3.1) are present in mouse neural sphere-derived progenitor cells[25,26].

Cai and colleagues demonstrated that multiple ion channels are heterogeneously expressed in rat embryonic neural stem cells, including I_A and IK_{DR} in > 80% of cells, I_{Na} (both TTX-sensitive and TTX-insensitive) and $I_{Ca.L}$ in a small population (22% and 19%) of neural stem cells[27]. IK_{DR} (encoded by Kv2.1) and I_A (encoded by Kv4.3) are also detected by Smith *et al*[28] in rat embryonic neural progenitor cells. Multiple ion channels, i.e. TTX-sensitive I_{Na}, TEA-insensitive IK_{DR} (likely encoded by Kv1.6, Kv2.1, and Kv2.2) and 4-AP-sensitive I_A (encoded by Kv4.2 and Kv4.3), are co-expressed in progenitor cells from neonatal rat forebrain[29]. However, only IK_{DR} encoded by Kv1.3 and Kv3.1 is present in adult rat neural progenitor cells[30]. Interestingly, 4-AP-sensitive I_A (encoded by Kv4.2) and α-dendrotoxin-sensitive IK_{DR} (likely encoded by Kv1.1, Kv1.6, and Kv3.1) are recently reported in human embryonic neural progenitor cells derived from aborted fetal brain tissue (12 weeks post-fertilization)[31]. Four types of ionic currents, I_A, IK_{DR}, I_{Kir} and $I_{Na.TTX}$, are also described by Lim *et al*[32] in human neural stem cells from aborted fetal cortex. In addition, a recent study reports that nifedipine-sensitive $I_{Ca.L}$ is expressed in neural stem/progenitor cells from the brain cortex of postnatal mice[33]. Moreover, TRPC1 has been found to mediate growth factor receptor-induced Ca^{2+} entry in embryonic rat neural stem cells[34].

ION CHANNELS IN CARDIAC PROGENITOR CELLS AND iPS CELLS

In cardiac progenitor cells, a recent study demonstrated that IK_{DR} (encoded by Kv1.1, Kv1.2 and Kv1.6), $I_{Cl.vol}$ (encoded by Clcn3) and I_{Kir} (encoded by Kir1.1, Kir2.1, and Kir2.2) are present in adult mouse cardiac c-kit$^+$ progenitor cells[35]. Only IK_{DR} (likely encoded by KCNQ2) is expressed in human iPS cells[36]. More information on ion channel expression in cardiac progenitor cells and iPS cells from different species is required.

ION CHANNELS IN CANCER STEM CELLS

Although cancer stem cells have been described in different types of cancers[37,38], information regarding ion channels in cancer stem cells is limited. A recent study reported that hERG (Kv11.1) channels are expressed in CD34$^+$/CD38$^-$/CD123(high) leukemia stem cells but not in normal bone marrow CD34$^+$ cells[39]. A high expression level of BK_{Ca} current has recently been recorded in CD133$^+$ stem cells from SH-SY5Y neuroblastoma[40]. Additional information remains to be collected on ion channel expression in stem cells from different types of cancer.

ROLES OF ION CHANNELS IN REGULATING PROLIFERATION AND/OR DIFFERENTIATION OF STEM CELLS

The effect of voltage-gated K^+ channels on cell mitogenesis was initially reported in human T lymphocytes by DeCoursey *et al*[41]. Great progress has been made in establishing the roles of specific channels in cell proliferation. K^+ channels modulate the cell progression through G0/G1 and K^+ channel expression changes with cell cycle progression.

Ion channels play an important role in controlling cell proliferation[42-44]. Kv channel blockade exhibits a significant anti-proliferative effect in numerous types of proliferative cells including glial cells, lymphocytes, endothelial cells, breast and prostate cancer cells[42,45]. These studies indicate that cell proliferation requires activity of K^+ channels. In addition, inhibition of voltage-gated K^+ channels and Na^+ channels suppresses migration of gastrointestinal epithelial cells[46,47]. It is believed that Kv, K_{Ca}, Na^+ and Cl^- channels mediate cancer cell migration, proliferation, invasion and metastasis[48].

We recently demonstrated that IK_{DR} is upregulated in early G1 phase while IK_{Ca} is increased in progressing G1 phase in rat bone marrow-derived MSCs. Silencing IK_{DR} channels or IK_{Ca} channels with corresponding short interference RNAs (siRNAs) targeting Kv1.2 and Kv2.1 or KCa3.1 inhibits cell proliferation and accumulates cells at G0/G1 phase[49], suggesting that IK_{DR} and IK_{Ca} are required for the regulation of cell proliferation in rat MSCs[49,50]. Blockade of IK_{DR} by 4-AP or TEA remarkably reduces proliferation of mouse and human ES cells[11], human iPS cells[36] and human fat tissue-derived MSCs[23] but not mouse cardiac c-kit$^+$ progenitor cells[35]. On the other hand, the inhibition of IK_{DR}, e.g. Kv1.3 by psora-4 or Kv3.1 by TEA, promotes proliferation of adult rat neural progenitor cells[25,26,30]. Also the blockade of IK_{DR}

by α-dendrotoxin is found to increase proliferation of human neural progenitor cells[31].

Blockade of IK_{Ca} with the selective blocker clotrimazole or silencing IK_{Ca} channel expression with KCa3.1 siRNA also reduces cell proliferation in mouse bone marrow-derived MSCs by accumulating cells at G0/G1 phase[51]. However, this is not the case for human fat tissue-derived MSCs in which the IK_{Ca} inhibition by clotrimazole has no inhibitory effect on cell proliferation[23].

The regulatory effect of BK_{Ca} on cell proliferation is dependent on cell type and/or experimental conditions. BK_{Ca} inhibition or KCa1.1 silencing reduces cell proliferation in human preadipocytes[52]. Block of BK_{Ca} by the selective channel blocker iberiotoxin inhibits cell proliferation in human endothelial cells[53,54] and in mouse ES cells[11] but not in human fat tissue-derived MSCs[23]. We recently found (unpublished) that inhibition of BK_{Ca} with paxilline or silencing BK_{Ca} with lentiviral-based short hairpin RNA targeting KCa1.1 reduces cell proliferation in human bone marrow-derived MSCs.

The volume-sensitive Cl^- channel ($I_{Cl.vol}$) has been implicated cell proliferation and apoptosis in a variety of cells[45,55,56]. We have found that $I_{Cl.vol}$ inhibition by the blocker 5-nitro-1-(3-phenylpropylamino) benzoic acid (NPPB) or silencing $I_{Cl.vol}$ channel with Clcn3 siRNA remarkably reduces cell proliferation in mouse MSCs by accumulating cells at G0/G1 phase, and the effect is mediated by suppressing cyclin D and cyclin E[51]. Similarly, block of $I_{Cl.vol}$ channel with NPPB also decreases cell proliferation in mouse cardiac c-kit$^+$ progenitor cells[35].

In proliferative cells, membrane hyperpolarization is implicated in silencing proliferation[54,55]. Membrane depolarization by the inhibition of I_{Kir} with Ba^{2+} or increase of extracellular K^+ concentration has been demonstrated to promote cell proliferation in adult neural progenitor cells[25]. This is consistent with the observation in astrocytes in which transient membrane depolarization with a reduction of Kir channel activity is observed during cell cycle progression from G1/S checkpoint to S phase[42]. However, this mechanism does not seem to be applicable for rat oligodendrocyte precursor cells. K_{ATP} openers diazoxide and pinacidil stimulate proliferation of rat oligodendrocyte precursor cells which is believed to be related to membrane hyperpolarization induced by K_{ATP}[57].

Limited information is available in literature regarding the physiological role of I_{to} (or I_A) in proliferative cells. We have recently found that inhibition of I_{to} by 4-AP or silencing Kv4.2 channel reduces cell proliferation in human preadipocytes[52]. Consistent with this observation, activation of I_A (Kv4.2) is found to be a prerequisite for cell proliferation in human embryonic neural progenitor cells[31].

Cytosolic Ca^{2+} activity is crucial for stem/progenitor cell cycle progression and growth[58,59]. Ca^{2+} entry through L-type Ca^{2+} channel is found to strongly correlate with differentiation of neural progenitor cells derived from mouse brain cortex; since nifedipine reduces while Bay K 8644 enhances neural differentiation[33]. In addition, TRPC1-mediated Ca^{2+} entry promotes differentiation of rat embryonic neural stem cells[34]. Silencing TRPC5 but not TRPC6 with corresponding siRNA decreases differentiation in rat neural progenitor cells[60]. These results suggest that cytosolic Ca^{2+} regulation by L-type Ca^{2+} channel, TRPC1 or TRPC5 channel plays an important role as a switch between proliferation and neuronal differentiation in different types of neural progenitor cells. It is interesting to note that a recent study demonstrated that TRPM7 channel is critical for the survival of mouse bone marrow derived mesenchymal stem cells[61].

While it is well recognized that voltage-gated TTX-sensitive (I_{NaTTX}) and TTX-resistant (I_{NaTTXR}, Nav1.5) Na^+ channels play a crucial role in generating action potential and conducting excitation impulse in excitable cells, the physiological function of I_{Na} is not fully understood in non-excitable and proliferative cells[16,27,62]. I_{Na} has been reported to regulate cell proliferation and migration in rat gastric epithelial cells[46,47] and human cancer cells[63,64]; however, blockade of I_{Na} by TTX does not affect cell proliferation in fat tissue-derived MSCs[23]. The effects of I_{Na} on proliferation, migration and/or differentiation remain to be studied in different types of stem cells.

CONCLUSION

Although multiple ion channels have been found to be heterogeneously present in different types of stem cells, it is not clear whether the heterogeneous expression of ion channels is due to different subpopulations of cells and/or different cell cycle phases. An effort has been made to study the relationship between ion channel expression and cell proliferation in different types of stem cells. It is generally believed that IK_{Ca} (KCa3.1) and $I_{Cl.vol}$ (Clcn3) are required for stem cell proliferation. Inhibition of IK_{DR} (encoded by Kv1.2, Kv1.3, Kv1.5, Kv1.6, Kv2.1, Kv3.1 or Kv10.1) reduces proliferation in ES cells and MSCs; however, blockade of some specific Kv channels, *e.g.* Kv1.3 by psora-4 or Kv3.1 by TEA in adult rat neural progenitor cells[30], Kv1.1, Kv1.6 and Kv3.1 by α-dendrotoxin in human neural progenitor cells[31], promotes cell proliferation. No effect on proliferation is observed with TEA or 4-AP inhibition of IK_{DR} (Kv1.1, Kv1.2 and Kv1.6) in mouse cardiac c-kit$^+$ progenitor cells[35]. Thus, the role of IK_{DR} in the regulation of proliferation is cell origin- and/or phenotype-dependent. Ion channels are believed to provide the basis for generating bioelectric signals that control migration, proliferation and differentiation in a variety of types of cells[55,65]. The studies summarized in this editorial indicate that patterns and phenotypes of ion channel expression in stem cells are species-, origin- and/or tissue-specific dependent. How these differences affect the cellular functions needs a detailed investigation in different type of stem cells. Further study should be focused on the effects of ion channels on migration and differentiation of different stem cells to determine which type of ion channel is involved in regulating cell migration and/or differentiation. This information is important for the study of regenerative medicine. Additional effort is required to investigate ion channels in cancer stem cells to locate potential therapeutic targets.

REFERENCES

1 **Takahashi K**, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell* 2006; **126**: 663-676
2 **Martin GR**. Isolation of a pluripotent cell line from early mouse embryos cultured in medium conditioned by teratocarcinoma stem cells. *Proc Natl Acad Sci USA* 1981; **78**: 7634-7638
3 **Evans MJ**, Kaufman MH. Establishment in culture of pluripotential cells from mouse embryos. *Nature* 1981; **292**: 154-156
4 **Becker AJ**, McCulloch EA, Till JE. Cytological demonstration of the clonal nature of spleen colonies derived from transplanted mouse marrow cells. *Nature* 1963; **197**: 452-454
5 **Smart N**, Riley PR. The stem cell movement. *Circ Res* 2008; **102**: 1155-1168
6 **Hanley J**, Rastegarlari G, Nathwani AC. An introduction to induced pluripotent stem cells. *Br J Haematol* 2010; **151**: 16-24
7 **Takahashi K**, Okita K, Nakagawa M, Yamanaka S. Induction of pluripotent stem cells from fibroblast cultures. *Nat Protoc* 2007; **2**: 3081-3089
8 **Park IH**, Zhao R, West JA, Yabuuchi A, Huo H, Ince TA, Lerou PH, Lensch MW, Daley GQ. Reprogramming of human somatic cells to pluripotency with defined factors. *Nature* 2008; **451**:141-166
9 **Yu J**, Hu K, Smuga-Otto K, Tian S, Stewart R, Slukvin II, Thomson JA. Human induced pluripotent stem cells free of vector and transgene sequences. *Science* 2009; **324**: 797-801
10 **Dick JE**. Stem cell concepts renew cancer research. *Blood* 2008; **112**: 4793-4807
11 **Wang K**, Xue T, Tsang SY, Van Huizen R, Wong CW, Lai KW, Ye Z, Cheng L, Au KW, Zhang J, Li GR, Lau CP, Tse HF, Li RA. Electrophysiological properties of pluripotent human and mouse embryonic stem cells. *Stem Cells* 2005; **23**: 1526-1534
12 **Ginis I**, Luo Y, Miura T, Thies S, Brandenberger R, Gerecht-Nir S, Amit M, Hoke A, Carpenter MK, Itskovitz-Eldor J, Rao MS. Differences between human and mouse embryonic stem cells. *Dev Biol* 2004; **269**: 360-380
13 **Hanna J**, Cheng AW, Saha K, Kim J, Lengner CJ, Soldner F, Cassady JP, Muffat J, Carey BW, Jaenisch R. Human embryonic stem cells with biological and epigenetic characteristics similar to those of mouse ESCs. *Proc Natl Acad Sci USA* 2010; **107**: 9222-9227
14 **Koestenbauer S**, Zech NH, Juch H, Vanderzwalmen P, Schoonjans L, Dohr G. Embryonic stem cells: similarities and differences between human and murine embryonic stem cells. *Am J Reprod Immunol* 2006; **55**: 169-180
15 **Heubach JF**, Graf EM, Leutheuser J, Bock M, Balana B, Zahanich I, Christ T, Boxberger S, Wettwer E, Ravens U. Electrophysiological properties of human mesenchymal stem cells. *J Physiol* 2004; **554**: 659-672
16 **Li GR**, Sun H, Deng X, Lau CP. Characterization of ionic currents in human mesenchymal stem cells from bone marrow. *Stem Cells* 2005; **23**: 371-382
17 **Kawano S**, Otsu K, Shoji S, Yamagata K, Hiraoka M. Ca(2+) oscillations regulated by Na(+)-Ca(2+) exchanger and plasma membrane Ca(2+) pump induce fluctuations of membrane currents and potentials in human mesenchymal stem cells. *Cell Calcium* 2003; **34**: 145-156
18 **Tang CY**, Bezanilla F, Papazian DM. Extracellular Mg(2+) modulates slow gating transitions and the opening of Drosophila ether-a-Go-Go potassium channels. *J Gen Physiol* 2000; **115**: 319-338
19 **Tao R**, Lau CP, Tse HF, Li GR. Functional ion channels in mouse bone marrow mesenchymal stem cells. *Am J Physiol Cell Physiol* 2007; **293**: C1561-C1567
20 **Li GR**, Deng XL, Sun H, Chung SS, Tse HF, Lau CP. Ion channels in mesenchymal stem cells from rat bone marrow. *Stem Cells* 2006; **24**: 1519-1528
21 **Deng XL**, Sun HY, Lau CP, Li GR. Properties of ion channels in rabbit mesenchymal stem cells from bone marrow. *Biochem Biophys Res Commun* 2006; **348**: 301-309
22 **Park KS**, Jung KH, Kim SH, Kim KS, Choi MR, Kim Y, Chai YG. Functional expression of ion channels in mesenchymal stem cells derived from umbilical cord vein. *Stem Cells* 2007; **25**: 2044-2052
23 **Bai X**, Ma J, Pan Z, Song YH, Freyberg S, Yan Y, Vykoukal D, Alt E. Electrophysiological properties of human adipose tissue-derived stem cells. *Am J Physiol Cell Physiol* 2007; **293**: C1539-C1550
24 **Attali B**, Wang N, Kolot A, Sobko A, Cherepanov V, Soliven B. Characterization of delayed rectifier Kv channels in oligodendrocytes and progenitor cells. *J Neurosci* 1997; **17**: 8234-8245
25 **Yasuda T**, Bartlett PF, Adams DJ. K(ir) and K(v) channels regulate electrical properties and proliferation of adult neural precursor cells. *Mol Cell Neurosci* 2008; **37**: 284-297
26 **Yasuda T**, Adams DJ. Physiological roles of ion channels in adult neural stem cells and their progeny. *J Neurochem* 2010; **114**: 946-959
27 **Cai J**, Cheng A, Luo Y, Lu C, Mattson MP, Rao MS, Furukawa K. Membrane properties of rat embryonic multipotent neural stem cells. *J Neurochem* 2004; **88**: 212-226
28 **Smith DO**, Rosenheimer JL, Kalil RE. Delayed rectifier and A-type potassium channels associated with Kv 2.1 and Kv 4.3 expression in embryonic rat neural progenitor cells. *PLoS One* 2008; **3**: e1604
29 **Stewart RR**, Zigova T, Luskin MB. Potassium currents in precursor cells isolated from the anterior subventricular zone of the neonatal rat forebrain. *J Neurophysiol* 1999; **81**: 95-102
30 **Liebau S**, Propper C, Bockers T, Lehmann-Horn F, Storch A, Grissmer S, Wittekindt OH. Selective blockage of Kv1.3 and Kv3.1 channels increases neural progenitor cell proliferation. *J Neurochem* 2006; **99**: 426-437
31 **Schaarschmidt G**, Wegner F, Schwarz SC, Schmidt H, Schwarz J. Characterization of voltage-gated potassium channels in human neural progenitor cells. *PLoS One* 2009; **4**: e6168
32 **Lim CG**, Kim SS, Suh-Kim H, Lee YD, Ahn SC. Characterization of ionic currents in human neural stem cells. *Korean J Physiol Pharmacol* 2008; **12**: 131-135
33 **D'Ascenzo M**, Piacentini R, Casalbore P, Budoni M, Pallini R, Azzena GB, Grassi C. Role of L-type Ca2+ channels in neural stem/progenitor cell differentiation. *Eur J Neurosci* 2006; **23**: 935-944
34 **Fiorio Pla A**, Maric D, Brazer SC, Giacobini P, Liu X, Chang YH, Ambudkar IS, Barker JL. Canonical transient receptor potential 1 plays a role in basic fibroblast growth factor (bFGF)/FGF receptor-1-induced Ca2+ entry and embryonic rat neural stem cell proliferation. *J Neurosci* 2005; **25**: 2687-2701
35 **Han Y**, Chen JD, Liu ZM, Zhou Y, Xia JH, Du XL, Jin MW. Functional ion channels in mouse cardiac c-kit(+) cells. *Am J Physiol Cell Physiol* 2010; **298**: C1109-C1117
36 **Jiang P**, Rushing SN, Kong CW, Fu J, Lieu DK, Chan CW, Deng W, Li RA. Electrophysiological properties of human induced pluripotent stem cells. *Am J Physiol Cell Physiol* 2010; **298**: C486-C495
37 **Frank NY**, Schatton T, Frank MH. The therapeutic promise of the cancer stem cell concept. *J Clin Invest* 2010; **120**: 41-50
38 **Park CY**, Tseng D, Weissman IL. Cancer stem cell-directed therapies: recent data from the laboratory and clinic. *Mol Ther* 2009; **17**: 219-230
39 **Li H**, Liu L, Guo L, Zhang J, Du W, Li X, Liu W, Chen X, Huang S. HERG K+ channel expression in CD34+/CD38-/CD123(high) cells and primary leukemia cells and analysis of its regulation in leukemia cells. *Int J Hematol* 2008; **87**: 387-392
40 **Park JH**, Park SJ, Chung MK, Jung KH, Choi MR, Kim Y, Chai YG, Kim SJ, Park KS. High expression of large-conductance Ca2+-activated K+ channel in the CD133+ subpopulation of SH-SY5Y neuroblastoma cells. *Biochem Biophys Res Commun* 2010; **396**: 637-642
41 **DeCoursey TE**, Chandy KG, Gupta S, Cahalan MD. Voltage-

gated K+ channels in human T lymphocytes: a role in mitogenesis? *Nature* 1984; **307**: 465-468
42 **MacFarlane SN**, Sontheimer H. Changes in ion channel expression accompany cell cycle progression of spinal cord astrocytes. *Glia* 2000; **30**: 39-48
43 **Wonderlin WF**, Strobl JS. Potassium channels, proliferation and G1 progression. *J Membr Biol* 1996; **154**: 91-107
44 **Pardo LA**. Voltage-gated potassium channels in cell proliferation. *Physiology* (Bethesda) 2004; **19**: 285-292
45 **Lang F**, Shumilina E, Ritter M, Gulbins E, Vereninov A, Huber SM. Ion channels and cell volume in regulation of cell proliferation and apoptotic cell death. *Contrib Nephrol* 2006; **152**: 142-160
46 **Wu WK**, Li GR, Wong TM, Wang JY, Yu L, Cho CH. Involvement of voltage-gated K+ and Na+ channels in gastric epithelial cell migration. *Mol Cell Biochem* 2008; **308**: 219-226
47 **Wu WK**, Li GR, Wong HP, Hui MK, Tai EK, Lam EK, Shin VY, Ye YN, Li P, Yang YH, Luo JC, Cho CH. Involvement of Kv1.1 and Nav1.5 in proliferation of gastric epithelial cells. *J Cell Physiol* 2006; **207**: 437-444
48 **Fraser SP**, Pardo LA. Ion channels: functional expression and therapeutic potential in cancer. Colloquium on Ion Channels and Cancer. *EMBO Rep* 2008; **9**: 512-515
49 **Deng XL**, Lau CP, Lai K, Cheung KF, Lau GK, Li GR. Cell cycle-dependent expression of potassium channels and cell proliferation in rat mesenchymal stem cells from bone marrow. *Cell Prolif* 2007; **40**: 656-670
50 **Wang SP**, Wang JA, Luo RH, Cui WY, Wang H. Potassium channel currents in rat mesenchymal stem cells and their possible roles in cell proliferation. *Clin Exp Pharmacol Physiol* 2008; **35**: 1077-1084
51 **Tao R**, Lau CP, Tse HF, Li GR. Regulation of cell proliferation by intermediate-conductance Ca2+-activated potassium and volume-sensitive chloride channels in mouse mesenchymal stem cells. *Am J Physiol Cell Physiol* 2008; **295**: C1409-C1416
52 **Hu H**, He ML, Tao R, Sun HY, Hu R, Zang WJ, Yuan BX, Lau CP, Tse HF, Li GR. Characterization of ion channels in human preadipocytes. *J Cell Physiol* 2009; **218**: 427-435
53 **Wiecha J**, Munz B, Wu Y, Noll T, Tillmanns H, Waldecker B. Blockade of Ca2+-activated K+ channels inhibits proliferation of human endothelial cells induced by basic fibroblast growth factor. *J Vasc Res* 1998; **35**: 363-371
54 **Kuhlmann CR**, Most AK, Li F, Munz BM, Schaefer CA, Walther S, Raedle-Hurst T, Waldecker B, Piper HM, Tillmanns H, Wiecha J. Endothelin-1-induced proliferation of human endothelial cells depends on activation of K+ channels and Ca2+ influx. *Acta Physiol Scand* 2005; **183**: 161-169
55 **Blackiston DJ**, McLaughlin KA, Levin M. Bioelectric controls of cell proliferation: ion channels, membrane voltage and the cell cycle. *Cell Cycle* 2009; **8**: 3519-3528
56 **Liu YJ**, Wang XG, Tang YB, Chen JH, Lv XF, Zhou JG, Guan YY. Simvastatin ameliorates rat cerebrovascular remodeling during hypertension via inhibition of volume-regulated chloride channel. *Hypertension* 2010; **56**: 445-452
57 **Fogal B**, McClaskey C, Yan S, Yan H, Rivkees SA. Diazoxide promotes oligodendrocyte precursor cell proliferation and myelination. *PLoS One* 2010; **5**: e10906
58 **Resende RR**, Adhikari A, da Costa JL, Lorencon E, Ladeira MS, Guatimosim S, Kihara AH, Ladeira LO. Influence of spontaneous calcium events on cell-cycle progression in embryonal carcinoma and adult stem cells. *Biochim Biophys Acta* 2010; **1803**: 246-260
59 **Ferreira-Martins J**, Rondon-Clavo C, Tugal D, Korn JA, Rizzi R, Padin-Iruegas ME, Ottolenghi S, De AA, Urbanek K, Ide-Iwata N, D'Amario D, Hosoda T, Leri A, Kajstura J, Anversa P, Rota M. Spontaneous calcium oscillations regulate human cardiac progenitor cell growth. *Circ Res* 2009; **105**: 764-774
60 **Shin HY**, Hong YH, Jang SS, Chae HG, Paek SL, Moon HE, Kim DG, Kim J, Paek SH, Kim SJ. A role of canonical transient receptor potential 5 channel in neuronal differentiation from A2B5 neural progenitor cells. *PLoS One* 2010; **5**: e10359
61 **Cheng H**, Feng JM, Figueiredo ML, Zhang H, Nelson PL, Marigo V, Beck A. Transient receptor potential melastatin type 7 channel is critical for the survival of bone marrow derived mesenchymal stem cells. *Stem Cells Dev* 2010; **19**: 1393-1403
62 **Li GR**, Sun HY, Chen JB, Zhou Y, Tse HF, Lau CP. Characterization of multiple ion channels in cultured human cardiac fibroblasts. *PLoS One* 2009; **4**: e7307
63 **Gao R**, Shen Y, Cai J, Lei M, Wang Z. Expression of voltage-gated sodium channel alpha subunit in human ovarian cancer. *Oncol Rep* 2010; **23**: 1293-1299
64 **Isbilen B**, Fraser SP, Djamgoz MB. Docosahexaenoic acid (omega-3) blocks voltage-gated sodium channel activity and migration of MDA-MB-231 human breast cancer cells. *Int J Biochem Cell Biol* 2006; **38**: 2173-2182
65 **Sundelacruz S**, Levin M, Kaplan DL. Role of membrane potential in the regulation of cell proliferation and differentiation. *Stem Cell Rev* 2009; **5**: 231-246

S- Editor Wang JL **L- Editor** Roemmele A **E- Editor** Ma WH

World Journal of Stem Cells

Online Submissions: http://www.wjgnet.com/1948-0210office
wjsc@wjgnet.com
www.wjgnet.com

World J Stem Cells 2011 March 26; 3(3): I
ISSN 1948-0210 (online)

Acknowledgments to reviewers of *World Journal of Stem Cells*

Many reviewers have contributed their expertise and time to the peer review, a critical process to ensure the quality of *World Journal of Stem Cells*. The editors and authors of the articles submitted to the journal are grateful to the following reviewers for evaluating the articles (including those published in this issue and those rejected for this issue) during the last editing time period.

Heli Teija Kristiina Skottman, PhD, Academy of Finland Research fellow, Regea Institute for Regenerative medicine, University of Tampere, Finland, Biokatu 12, 33520 Tampere, Finland

Soren Paludan Sheikh, MD, PhD, Professor, Department of Biochemistry, Pharmacology and Genetics, Odense Univsersity Hospital, University of Southern Denmark, Sdr. Boulevard 29, DK 5000, Denmark

Andre Van Wijnen, PhD, Department of Cell Biology, Rm S3-322, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA 01655, United States

Ludwig Aigner, PhD, Professor, Institute of Molecular Regenerative Medicine, Paracelsus Medical University, Strubergasse 21, A-5020 Salzburg, Austria

Borhane Annabi, PhD, Professor, Department of Chemistry, Biomed Research Centre, Université du Québec à Montréal Montreal, Quebec, H2X 2J6, Canada

Denis Corbeil, PhD, Tissue Engineering Laboratories, Biotec, Medical Faculty, Technical University of Dresden, Tatzberg 47-49, 01307, Dresden, Germany

Yusuke Furukawa, MD, PhD, Division of Stem Cell Regulation, Center for Molecular Medicine, Jichi Medical University School of Medicine, 3311-1 Yakushiji, Shimotsuke, Tochigi 329-0498, Japan

Mieke Geens, PhD, EMGE, UZ Brussel, Laarbeeklaan 101, 1090 Jette, Brussels, Belgium

Zhong-Chao Han, MD, PhD, Professor, Institute of Hematology, Chinese Academy of Medical Sciences and Peking Union Medical College, Tianjin 300020, China

Xiao-Yan Jiang, MD, PhD, Associate Professor, Medical Genetics, University of British Columbia, Senior Scientist, Terry Fox Laboratory, BC Cancer Agency Research Centre, 675 West 10th Avenue, Vancouver, BC V5Z 1L3, Canada

Hiroyuki Miyoshi, PhD, Subteam for Manipulation of Cell Fate, BioResourceCenter, RIKEN, 3-1-1 Koyadai, Tsukuba, Ibaraki 305-0074, Japan

Alice Pébay, PhD, Centre for Neuroscience & Department of Pharmacology, University of Melbourne, Parkville VIC 3010, Australia

John F Zhong, PhD, Assistant Professor, School of Medicine, University of Southern California, 2025 Zonal Ave, RMR 210, Los Angeles, CA 90033, United States

Hong Yu, PhD, Miami VA Health Care System, 1201 NW 16th St, Research 151, Miami, FL 33125, United States

World Journal of Stem Cells

Online Submissions: http://www.wjgnet.com/1948-0210office
wjsc@wjgnet.com
www.wjgnet.com

World J Stem Cells 2011 March 26; 3(3): I
ISSN 1948-0210 (online)

Meetings

Events Calendar 2011

March 26, 2011
Stem Cell Agency Governance Subcommittee Meeting, Crowne Plaza SFO, 1177 Airport Blvd, Burlingame, CA, United States

January 29-February 2, 2011
LabAutomation2011, Palm Springs, CA, United States

February 4, 2011
7th annual Swiss Stem Cell Network meeting, Swiss Federal Institute of Technology in Lausanne, Switzerland

March 1, 2011
The 6th Annual Stem Cell Summit, 11 Fulton Street, New York City, NY, United States

March 22, 2011
StemCONN 2011, Farmington, CT, United States

March 27-31, 2011
SBS 17th Annual Conference and Exhibition, Orlando, FL, United States

April 6-8, 2011
EMBO Conference-Advances in Stem Cell Research: Development, Regeneration and Disease, Institut Pasteur, Paris, France

April 7-10, 2011
2011 CSHL Meeting on Stem Cell Engineering & Cell Therapy, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States

April 25-26, 2011
International Conference on Stem Cell Research, Hotel Equatorial Penang, Malaysia

April 27, 2011
6th Annual Wisconsin Stem Cell Symposium, BioPharmaceutical Technology Center, Madison, WI, United States

May 9-11, 2011
The World Stem Cells and Regenerative Medicine Congress 2011, Victoria Park Plaza, London, United Kingdom

May 23-24, 2011
The 4th Annual Israeli Stem Cell Meeting, Beit Sourasky, Chaim Sheba Medical Center, Israel

May 26-27, 2011
7th annual Stem Cell Research & Therapeutics Conference, Boston, MA, United States

September 20-24, 2011
2011 CSHL Meeting on Stem Cell Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States

October 2011
3rd Annual World Stem Cells & Regenerative Medicine Congress Asia 2011, Seoul, South Korea

WJSC World Journal of Stem Cells

Online Submissions: http://www.wjgnet.com/1948-0210office
wjsc@wjgnet.com
www.wjgnet.com

World J Stem Cells 2011 March 26; 3(3): I-V
ISSN 1948-0210 (online)

Instructions to authors

GENERAL INFORMATION

World Journal of Stem Cells (*World J Stem Cells*, *WJSC*, online ISSN 1948-0210, DOI: 10.4252), is a monthly, open-access (OA), peer-reviewed journal supported by an editorial board of 284 experts in stem cell from 28 countries.

The biggest advantage of the OA model is that it provides free, full-text articles in PDF and other formats for experts and the public without registration, which eliminates the obstacle that traditional journals possess and usually delays the speed of the propagation and communication of scientific research results. The open access model has been proven to be a true approach that may achieve the ultimate goal of the journals, i.e. the maximization of the value to the readers, authors and society.

Maximization of personal benefits

The role of academic journals is to exhibit the scientific levels of a country, a university, a center, a department, and even a scientist, and build an important bridge for communication between scientists and the public. As we all know, the significance of the publication of scientific articles lies not only in disseminating and communicating innovative scientific achievements and academic views, as well as promoting the application of scientific achievements, but also in formally recognizing the "priority" and "copyright" of innovative achievements published, as well as evaluating research performance and academic levels. So, to realize these desired attributes of *WJSC* and create a well-recognized journal, the following four types of personal benefits should be maximized. The maximization of personal benefits refers to the pursuit of the maximum personal benefits in a well-considered optimal manner without violation of the laws, ethical rules and the benefits of others. (1) Maximization of the benefits of editorial board members: The primary task of editorial board members is to give a peer review of an unpublished scientific article *via* online office system to evaluate its innovativeness, scientific and practical values and determine whether it should be published or not. During peer review, editorial board members can also obtain cutting-edge information in that field at first hand. As leaders in their field, they have priority to be invited to write articles and publish commentary articles. We will put peer reviewers' names and affiliations along with the article they reviewed in the journal to acknowledge their contribution; (2) Maximization of the benefits of authors: Since *WJSC* is an open-access journal, readers around the world can immediately download and read, free of charge, high-quality, peer-reviewed articles from *WJSC* official website, thereby realizing the goals and significance of the communication between authors and peers as well as public reading; (3) Maximization of the benefits of readers: Readers can read or use, free of charge, high-quality peer-reviewed articles without any limits, and cite the arguments, viewpoints, concepts, theories, methods, results, conclusion or facts and data of pertinent literature so as to validate the innovativeness, scientific and practical values of their own research achievements, thus ensuring that their articles have novel arguments or viewpoints, solid evidence and correct conclusion; and (4) Maximization of the benefits of employees: It is an iron law that a first-class journal is unable to exist without first-class editors, and only first-class editors can create a first-class academic journal. We insist on strengthening our team cultivation and construction so that every employee, in an open, fair and transparent environment, could contribute their wisdom to edit and publish high-quality articles, thereby realizing the maximization of the personal benefits of editorial board members, authors and readers, and yielding the greatest social and economic benefits.

Aims and scope

The major task of *WJSC* is to report rapidly original articles and comprehensive reviews on basic laboratory investigations of stem cells and their application in clinical care and treatment of patients. *WJSC* is designed to cover all aspects of stem cells, including: Embryonic, neural, hematopoietic, mesenchymal, tissue-specific, and cancer stem cells; the stem cell niche; stem cell genomics and proteomics; and stem cell techniques and their application in clinical trials. Papers published in *WJSC* will cover the biology, culture, differentiation and application of stem cells from all stages of their development, from germ cell to embryo and adult.

Columns

The columns in the issues of *WJSC* will include: (1) Editorial: To introduce and comment on major advances and developments in the field; (2) Frontier: To review representative achievements, comment on the state of current research, and propose directions for future research; (3) Topic Highlight: This column consists of three formats, including (A) 10 invited review articles on a hot topic, (B) a commentary on common issues of this hot topic, and (C) a commentary on the 10 individual articles; (4) Observation: To update the development of old and new questions, highlight unsolved problems, and provide strategies on how to solve the questions; (5) Guidelines for Basic Research: To provide guidelines for basic research; (6) Guidelines for Clinical Practice: To provide guidelines for clinical diagnosis and treatment; (7) Review: To review systemically progress and unresolved problems in the field, comment on the state of current research, and make suggestions for future work; (8) Original Articles: T To report innovative and original findings in stem cells; (9) Brief Articles: To briefly report the novel and innovative findings in stem cells; (10) Case Report: To report a rare or typical case; (11) Letters to the Editor: To discuss and make reply to the contributions published in *WJSC*, or to introduce and comment on a controversial issue of general interest; (12) Book Reviews: To introduce and comment on quality monographs of stem cells; and (13) Guidelines: To introduce consensuses and guidelines reached by international and national academic authorities worldwide on the research in stem cells.

Name of journal

World Journal of Stem Cells

Serial publication number

ISSN 1948-0210 (online)

Indexed and Abstracted in

PubMed Central, PubMed, Digital Object Identifer, and Directory of Open Access Journals.

Published by

Baishideng Publishing Group Co., Limited

SPECIAL STATEMENT

All articles published in this journal represent the viewpoints of the authors except where indicated otherwise.

Biostatistical editing

Statisital review is performed after peer review. We invite an expert in Biomedical Statistics from to evaluate the statistical method used in the paper, including *t*-test (group or paired comparisons), chi-squared test, Ridit, probit, logit, regression (linear, curvilinear, or stepwise), correlation, analysis of variance, analysis of covariance, *etc*. The reviewing points include: (1) Statistical methods should be described when they are used to verify the results; (2) Whether the statistical techniques are suitable or correct; (3) Only homogeneous data can be averaged. Standard deviations are preferred to standard errors. Give the number of observations and subjects (*n*). Losses in observations, such as drop-outs from the study should be reported; (4) Values such as ED50, LD50, IC50 should have their 95% confidence limits calculated and compared by weighted probit analysis (Bliss and Finney); and (5) The word 'significantly' should be replaced by its synonyms (if it indicates extent) or the *P* value (if it indicates statistical significance).

Conflict-of-interest statement

In the interests of transparency and to help reviewers assess any potential bias, *WJSC* requires authors of all papers to declare any competing commercial, personal, political, intellectual, or religious interests in relation to the submitted work. Referees are also asked to indicate any potential conflict they might have reviewing a particular paper. Before submitting, authors are suggested to read "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Ethical Considerations in the Conduct and Reporting of Research: Conflicts of Interest" from International Committee of Medical Journal Editors (ICMJE), which is available at: http://www.icmje.org/ethical_4conflicts.html.

Sample wording: [Name of individual] has received fees for serving as a speaker, a consultant and an advisory board member for [names of organizations], and has received research funding from [names of organization]. [Name of individual] is an employee of [name of organization]. [Name of individual] owns stocks and shares in [name of organization]. [Name of individual] owns patent [patent identification and brief description].

Statement of informed consent

Manuscripts should contain a statement to the effect that all human studies have been reviewed by the appropriate ethics committee or it should be stated clearly in the text that all persons gave their informed consent prior to their inclusion in the study. Details that might disclose the identity of the subjects under study should be omitted. Authors should also draw attention to the Code of Ethics of the World Medical Association (Declaration of Helsinki, 1964, as revised in 2004).

Statement of human and animal rights

When reporting the results from experiments, authors should follow the highest standards and the trial should comform to Good Clinical Practice (for example, US Food and Drug Administration Good Clinical Practice in FDA-Regulated Clinical Trials; UK Medicines Research Council Guidelines for Good Clinical Practice in Clinical Trials) and/or the World Medical Association Declaration of Helsinki. Generally, we suggest authors follow the lead investigator's national standard. If doubt exists whether the research was conducted in accordance with the above standards, the authors must explain the rationale for their approach and demonstrate that the institutional review body explicitly approved the doubtful aspects of the study.

Before submitting, authors should make their study approved by the relevant research ethics committee or institutional review board. If human participants were involved, manuscripts must be accompanied by a statement that the experiments were undertaken with the understanding and appropriate informed consent of each. Any personal item or information will not be published without explicit consents from the involved patients. If experimental animals were used, the materials and methods (experimental procedures) section must clearly indicate that appropriate measures were taken to minimize pain or discomfort, and details of animal care should be provided.

SUBMISSION OF MANUSCRIPTS

Manuscripts should be typed in 1.5 line spacing and 12 pt. Book Antiqua with ample margins. Number all pages consecutively, and start each of the following sections on a new page: Title Page, Abstract, Introduction, Materials and Methods, Results, Discussion, Acknowledgements, References, Tables, Figures, and Figure Legends. Neither the editors nor the publisher are responsible for the opinions expressed by contributors. Manuscripts formally accepted for publication become the permanent property of Baishideng Publishing Group Co., Limited, and may not be reproduced by any means, in whole or in part, without the written permission of both the authors and the publisher. We reserve the right to copy-edit and put onto our website accepted manuscripts. Authors should follow the relevant guidelines for the care and use of laboratory animals of their institution or national animal welfare committee. For the sake of transparency in regard to the performance and reporting of clinical trials, we endorse the policy of the ICMJE to refuse to publish papers on clinical trial results if the trial was not recorded in a publicly-accessible registry at its outset. The only register now available, to our knowledge, is http://www.clinicaltrials.gov sponsored by the United States National Library of Medicine and we encourage all potential contributors to register with it. However, in the case that other registers become available you will be duly notified. A letter of recommendation from each author's organization should be provided with the contributed article to ensure the privacy and secrecy of research is protected.

Authors should retain one copy of the text, tables, photographs and illustrations because rejected manuscripts will not be returned to the author(s) and the editors will not be responsible for loss or damage to photographs and illustrations sustained during mailing.

Online submissions

Manuscripts should be submitted through the Online Submission System at: http://www.wjgnet.com/1948-0210office. Authors are highly recommended to consult the ONLINE INSTRUCTIONS TO AUTHORS (http://www.wjgnet.com/1948-0210/g_info_20100313165700.htm) before attempting to submit online. For assistance, authors encountering problems with the Online Submission System may send an email describing the problem to wjsc@wjgnet.com, or by telephone: +86-10-85381891. If you submit your manuscript online, do not make a postal contribution. Repeated online submission for the same manuscript is strictly prohibited.

MANUSCRIPT PREPARATION

All contributions should be written in English. All articles must be submitted using word-processing software. All submissions must be typed in 1.5 line spacing and 12 pt. Book Antiqua with ample margins. Style should conform to our house format. Required information for each of the manuscript sections is as follows:

Title page

Title: Title should be less than 12 words.

Running title: A short running title of less than 6 words should be provided.

Authorship: Authorship credit should be in accordance with the standard proposed by International Committee of Medical Journal Editors, based on (1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published. Authors should meet conditions 1, 2, and 3.

Institution: Author names should be given first, then the complete name of institution, city, province and postcode. For example, Xu-Chen Zhang, Li-Xin Mei, Department of Pathology, Chengde Medical College, Chengde 067000, Hebei Province, China. One author may be represented from two institutions, for example, George

Sgourakis, Department of General, Visceral, and Transplantation Surgery, Essen 45122, Germany; George Sgourakis, 2nd Surgical Department, Korgialenio-Benakio Red Cross Hospital, Athens 15451, Greece

Author contributions: The format of this section should be: Author contributions: Wang CL and Liang L contributed equally to this work; Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research; Wang CL, Zou CC, Hong F and Wu XM performed the research; Xue JZ and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed the data; and Wang CL, Liang L and Fu JF wrote the paper.

Supportive foundations: The complete name and number of supportive foundations should be provided, e.g. Supported by National Natural Science Foundation of China, No. 30224801

Correspondence to: Only one corresponding address should be provided. Author names should be given first, then author title, affiliation, the complete name of institution, city, postcode, province, country, and email. All the letters in the email should be in lower case. A space interval should be inserted between country name and email address. For example, Montgomery Bissell, MD, Professor of Medicine, Chief, Liver Center, Gastroenterology Division, University of California, Box 0538, San Francisco, CA 94143, United States. montgomery.bissell@ucsf.edu

Telephone and fax: Telephone and fax should consist of +, country number, district number and telephone or fax number, e.g. Telephone: +86-10-85381891 Fax: +86-10-85381893

Peer reviewers: All articles received are subject to peer review. Normally, three experts are invited for each article. Decision for acceptance is made only when at least two experts recommend an article for publication. Reviewers for accepted manuscripts are acknowledged in each manuscript, and reviewers of articles which were not accepted will be acknowledged at the end of each issue. To ensure the quality of the articles published in *WJSC*, reviewers of accepted manuscripts will be announced by publishing the name, title/position and institution of the reviewer in the footnote accompanying the printed article. For example, reviewers: Professor Jing-Yuan Fang, Shanghai Institute of Digestive Disease, Shanghai, Affiliated Renji Hospital, Medical Faculty, Shanghai Jiaotong University, Shanghai, China; Professor Xin-Wei Han, Department of Radiology, The First Affiliated Hospital, Zhengzhou University, Zhengzhou, Henan Province, China; and Professor Anren Kuang, Department of Nuclear Medicine, Huaxi Hospital, Sichuan University, Chengdu, Sichuan Province, China.

Abstract

There are unstructured abstracts (no more than 256 words) and structured abstracts (no more than 480). The specific requirements for structured abstracts are as follows:

An informative, structured abstracts of no more than 480 words should accompany each manuscript. Abstracts for original contributions should be structured into the following sections. AIM (no more than 20 words): Only the purpose should be included. Please write the aim as the form of "To investigate/study/…; MATERIALS AND METHODS (no more than 140 words); RESULTS (no more than 294 words): You should present *P* values where appropriate and must provide relevant data to illustrate how they were obtained, e.g. 6.92 ± 3.86 *vs* 3.61 ± 1.67, $P < 0.001$; CONCLUSION (no more than 26 words).

Key words

Please list 5-10 key words, selected mainly from *Index Medicus*, which reflect the content of the study.

Text

For articles of these sections, original articles and brief articles, the main text should be structured into the following sections: INTRODUCTION, MATERIALS AND METHODS, RESULTS and DISCUSSION, and should include appropriate Figures and Tables. Data should be presented in the main text or in Figures and Tables, but not in both. The main text format of these sections, editorial, topic highlight, case report, letters to the editors, can be found at: http://www.wjgnet.com/1948-0210/g_info_list.htm.

Illustrations

Figures should be numbered as 1, 2, 3, *etc.*, and mentioned clearly in the main text. Provide a brief title for each figure on a separate page. Detailed legends should not be provided under the figures. This part should be added into the text where the figures are applicable. Figures should be either Photoshop or Illustrator files (in tiff, eps, jpeg formats) at high-resolution. Examples can be found at: http://www.wjgnet.com/1007-9327/13/4520.pdf; http://www.wjgnet.com/1007-9327/13/4554.pdf; http://www.wjgnet.com/1007-9327/13/4891.pdf; http://www.wjgnet.com/1007-9327/13/4986.pdf; http://www.wjgnet.com/1007-9327/13/4498.pdf. Keeping all elements compiled is necessary in line-art image. Scale bars should be used rather than magnification factors, with the length of the bar defined in the legend rather than on the bar itself. File names should identify the figure and panel. Avoid layering type directly over shaded or textured areas. Please use uniform legends for the same subjects. For example: Figure 1 Pathological changes in atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: …*etc.* It is our principle to publish high resolution-figures for the printed and E-versions.

Tables

Three-line tables should be numbered 1, 2, 3, *etc.*, and mentioned clearly in the main text. Provide a brief title for each table. Detailed legends should not be included under tables, but rather added into the text where applicable. The information should complement, but not duplicate the text. Use one horizontal line under the title, a second under column heads, and a third below the Table, above any footnotes. Vertical and italic lines should be omitted.

Notes in tables and illustrations

Data that are not statistically significant should not be noted. $^{a}P < 0.05$, $^{b}P < 0.01$ should be noted ($P > 0.05$ should not be noted). If there are other series of *P* values, $^{c}P < 0.05$ and $^{d}P < 0.01$ are used. A third series of *P* values can be expressed as $^{e}P < 0.05$ and $^{f}P < 0.01$. Other notes in tables or under illustrations should be expressed as ^{1}F, ^{2}F, ^{3}F; or sometimes as other symbols with a superscript (Arabic numerals) in the upper left corner. In a multi-curve illustration, each curve should be labeled with ●, ○, ■, □, ▲, △, *etc.*, in a certain sequence.

Acknowledgments

Brief acknowledgments of persons who have made genuine contributions to the manuscript and who endorse the data and conclusions should be included. Authors are responsible for obtaining written permission to use any copyrighted text and/or illustrations.

REFERENCES

Coding system

The author should number the references in Arabic numerals according to the citation order in the text. Put reference numbers in square brackets in superscript at the end of citation content or after the cited author's name. For citation content which is part of the narration, the coding number and square brackets should be typeset normally. For example, "Crohn's disease (CD) is associated with increased intestinal permeability[1,2]". If references are cited directly in the text, they should be put together within the text, for example, "From references[19,22-24], we know that..."

When the authors write the references, please ensure that the order in text is the same as in the references section, and also ensure the spelling accuracy of the first author's name. Do not list the same citation twice.

PMID and DOI

Pleased provide PubMed citation numbers to the reference list, e.g. PMID and DOI, which can be found at http://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed and http://www.crossref.org/SimpleTextQuery/, respectively. The numbers will be used in E-version of this journal.

Style for journal references

Authors: the name of the first author should be typed in bold-faced letters. The family name of all authors should be typed with the initial letter capitalized, followed by their abbreviated first and middle initials. (For example, Lian-Sheng Ma is abbreviated as Ma LS, Bo-Rong Pan as Pan BR). The title of the cited article and italicized journal title (journal title should be in its abbreviated form as shown in PubMed), publication date, volume number (in black), start page, and end page [PMID: 11819634 DOI: 10.3748/wjg.13.5396].

Style for book references

Authors: the name of the first author should be typed in bold-faced letters. The surname of all authors should be typed with the initial letter capitalized, followed by their abbreviated middle and first initials. (For example, Lian-Sheng Ma is abbreviated as Ma LS, Bo-Rong Pan as Pan BR) Book title. Publication number. Publication place: Publication press, Year: start page and end page.

Format

Journals

English journal article (list all authors and include the PMID where applicable)

1 **Jung EM**, Clevert DA, Schreyer AG, Schmitt S, Rennert J, Kubale R, Feuerbach S, Jung F. Evaluation of quantitative contrast harmonic imaging to assess malignancy of liver tumors: A prospective controlled two-center study. *World J Gastroenterol* 2007; **13**: 6356-6364 [PMID: 18081224 DOI: 10.3748/wjg.13.6356]

Chinese journal article (list all authors and include the PMID where applicable)

2 **Lin GZ**, Wang XZ, Wang P, Lin J, Yang FD. Immunologic effect of Jianpi Yishen decoction in treatment of Pixu-diarrhoea. *Shijie Huaren Xiaohua Zazhi* 1999; **7**: 285-287

In press

3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

Organization as author

4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMCID:2516377 DOI:10.1161/01.HYP.0000035706.28494.09]

Both personal authors and an organization as author

5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

No author given

6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

Volume with supplement

7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/j.1526-4610.42.s2.7.x]

Issue with no volume

8 **Banit DM**, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. *Clin Orthop Relat Res* 2002; (**401**): 230-238 [PMID: 12151900 DOI:10.1097/00003086-200208000-00026]

No volume or issue

9 Outreach: Bringing HIV-positive individuals into care. *HRSA Careaction* 2002; 1-6 [PMID: 12154804]

Books

Personal author(s)

10 **Sherlock S**, Dooley J. Diseases of the liver and billiary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

Chapter in a book (list all authors)

11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

Author(s) and editor(s)

12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

Conference proceedings

13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

Conference paper

14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

Electronic journal (list all authors)

15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: http://www.cdc.gov/ncidod/eid/index.htm

Patent (list all authors)

16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

Statistical data

Write as mean ± SD or mean ± SE.

Statistical expression

Express *t* test as *t* (in italics), *F* test as *F* (in italics), chi square test as χ^2 (in Greek), related coefficient as *r* (in italics), degree of freedom as υ (in Greek), sample number as *n* (in italics), and probability as *P* (in italics).

Units

Use SI units. For example: body mass, m (B) = 78 kg; blood pressure, p (B) = 16.2/12.3 kPa; incubation time, t (incubation) = 96 h, blood glucose concentration, c (glucose) 6.4 ± 2.1 mmol/L; blood CEA mass concentration, p (CEA) = 8.6 24.5 μg/L; CO_2 volume fraction, 50 mL/L CO_2, not 5% CO_2; likewise for 40 g/L formaldehyde, not 10% formalin; and mass fraction, 8 ng/g, *etc.* Arabic numerals such as 23, 243, 641 should be read 23 243 641.

The format for how to accurately write common units and quantums can be found at: http://www.wjgnet.com/1948-0210/g_info_20100313172144.htm.

Abbreviations

Standard abbreviations should be defined in the abstract and on first mention in the text. In general, terms should not be abbreviated unless they are used repeatedly and the abbreviation is helpful to the reader. Permissible abbreviations are listed in Units, Symbols and Abbreviations: A Guide for Biological and Medical Editors and Authors (Ed. Baron DN, 1988) published by The Royal Society of Medicine, London. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, mAb, can be used directly without further explanation.

Italics
Quantities: *t* time or temperature, *c* concentration, *A* area, *l* length, *m* mass, *V* volume.
Genotypes: *gyrA*, *arg* 1, *c myc*, *c fos*, *etc.*
Restriction enzymes: *Eco*RI, *Hin*dI, *Bam*HI, *Kbo* I, *Kpn* I, *etc.*
Biology: *H. pylori*, *E coli*, *etc.*

Examples for paper writing
Editorial: http://www.wjgnet.com/1948-0210/g_info_20100313165833.htm

Frontier: http://www.wjgnet.com/1948-0210/g_info_20100313170509.htm

Topic highlight: http://www.wjgnet.com/1948-0210/g_info_20100313170618.htm

Observation: http://www.wjgnet.com/1948-0210/g_info_20100313170727.htm

Guidelines for basic research: http://www.wjgnet.com/1948-0210/g_info_20100313170855.htm

Guidelines for clinical practice: http://www.wjgnet.com/1948-0210/g_info_20100313171012.htm

Review: http://www.wjgnet.com/1948-0210/g_info_20100313171124.htm

Original articles: http://www.wjgnet.com/1948-0210/g_info_20100313171239.htm

Brief articles: http://www.wjgnet.com/1948-0210/g_info_20100313171358.htm

Case report: http://www.wjgnet.com/1948-0210/g_info_20100313171504.htm

Letters to the editor: http://www.wjgnet.com/1948-0210/g_info_20100313171613.htm

Book reviews: http://www.wjgnet.com/1948-0210/g_info_20100313171713.htm

Guidelines: http://www.wjgnet.com/1948-0210/g_info_20100313171803.htm

SUBMISSION OF THE REVISED MANUSCRIPTS AFTER ACCEPTED

Please revise your article according to the revision policies of *WJSC*. The revised version including manuscript and high-resolution image figures (if any) should be copied on a floppy or compact disk. The author should send the revised manuscript, along with printed high-resolution color or black and white photos, copyright transfer letter, and responses to the reviewers by courier (such as EMS/DHL).

Editorial Office

World Journal of Stem Cells
Editorial Department: Room 903, Building D,
Ocean International Center, No. 62 Dongsihuan Zhonglu,
Chaoyang District, Beijing 100025, China
E-mail: wjsc@wjgnet.com
http://www.wjgnet.com
Telephone: +86-10-85381891
Fax: +86-10-85381893

Language evaluation
The language of a manuscript will be graded before it is sent for revision. (1) Grade A: priority publishing; (2) Grade B: minor language polishing; (3) Grade C: a great deal of language polishing needed; and (4) Grade D: rejected. Revised articles should reach Grade A or B.

Copyright assignment form
Please download a Copyright assignment form from http://www.wjgnet.com/1948-0210/g_info_20100313172045.htm.

Responses to reviewers
Please revise your article according to the comments/suggestions provided by the reviewers. The format for responses to the reviewers' comments can be found at: http://www.wjgnet.com/1948-0210/g_info_20100313172000.htm.

Proof of financial support
For paper supported by a foundation, authors should provide a copy of the document and serial number of the foundation.

Links to documents related to the manuscript
WJSC will be initiating a platform to promote dynamic interactions between the editors, peer reviewers, readers and authors. After a manuscript is published online, links to the PDF version of the submitted manuscript, the peer-reviewers' report and the revised manuscript will be put on-line. Readers can make comments on the peer reviewer's report, authors' responses to peer reviewers, and the revised manuscript. We hope that authors will benefit from this feedback and be able to revise the manuscript accordingly in a timely manner.

Science news releases
Authors of accepted manuscripts are suggested to write a science news item to promote their articles. The news will be released rapidly at EurekAlert/AAAS (http://www.eurekalert.org). The title for news items should be less than 90 characters; the summary should be less than 75 words; and main body less than 500 words. Science news items should be lawful, ethical, and strictly based on your original content with an attractive title and interesting pictures.

Publication fee
WJSC is an international, peer-reviewed, Open-Access, online journal. Articles published by this journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license. Authors of accepted articles must pay a publication fee. The related standards are as follows. Publication fee: 1300 USD per article. Editorial, topic highlights, book reviews and letters to the editor are published free of charge.