Clinical and laboratory features of mesenchymal stromal cells in pediatric stem cell transplantation

Ball, L.M.

Curriculum vitae

Lynne Margaret Ball was born in Whiston, Lancashire on 12th September 1953, the youngest of six children. She was educated at Notre Dame Grammar School for Girls, Eccelston, St Helens, Lancashire and having achieved nine ordinary level and four advanced level GCE certificates in 1972, she went on to study medicine at the Royal Free Hospital Medical School, London University in 1974. In her pre-clinical studies she gained certificates of merit in both physiology and biochemistry.

Following certification in prize medicine and surgery examinations, she qualified in 1979 and continued her medical training in Cambridge, Glasgow, Liverpool and London. She trained and examined and gained her fellowship of the Royal College of Physicians, then the Royal College of Pathologists (specialist subject Hematology) and finally as a Fellow of the Royal College of Pediatrics and Child Health.

She specialized in pediatric hemato-oncology and bone marrow transplantation with her appointment as pediatric registrar in Glasgow followed by her appointment as lecturer in Guilford Street Center for Child Health University of London and as honorary senior registrar at Great Ormond Street Hospital for Sick Children, London in 1986. She was appointed Consultant Head of Department Pediatric Hematology and Bone Marrow Transplantation at Alder Hey Children's Hospital Liverpool in October 1988.

She re-located to Canada as Associate Professor in Pediatrics and Hematology, Dalhousie University, Halifax, Nova Scotia in December 1995 and later undertook a 12 months sabbatical as a pediatric hemato-oncologist in the West Indies University, Trinidad and Tobago.

In November 1999, she was invited by the then head of IHOBA, Professor Dr. J. Vossen, to join the hematology, oncology and bone marrow transplant unit (IHOBA), Department of Pediatrics Leiden University Medical Center Leiden, the Netherlands as Senior Medical Academic Specialist, where she continues in her full time function to the present day.

Her interests are in malignant hematological diseases of childhood as well as hematopoietic stem cell transplantation, especially alternative stem cell sources. She is actively pursuing scientific investigations into the properties of mesenchymal stem cells in children with malignant and autoimmune disease, as well as developing clinical studies into the use of mesenchymal stem cells for transplantation and immune modulation.

She is also active in pediatric palliative care in the Netherlands.

She has published more than fifty referenced articles, over referenced 250 abstracts as well as five chapters in books.

She is an active member of many national as well as international organizations affiliated to cancer care in children and young adults.

She is married to Dick with one daughter Hannah, three step daughters Hester, Liselot and Leonore, together with five step-grandchildren, Noah, Christel, Miko, Jannick and Milou.

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Historical footnote

"Disease is very old, and nothing about it has changed. It is we who change, as we learn to recognize what was formerly imperceptible"

- Jean Martin Charcot (1825-1893)
De léxpectation en medicine

MSC and tissue repair 1060

From: 11th century manuscript Táin Bó Cúalnge (Cattle Raid of Cooley) from the Lebor Laignech Book of Leinster, English translation (1914) by Joseph Dunn, London: Irish translation Die Altirische Heldensage Táin Bó Cúalnge (1905) by Ernst Windisch, Leipzig: Verlag von S. Hirzel.

Nevertheless Fingin the prophet-physician gave his choice to Cethern son of Fintan: A long illness for him and afterwards to obtain help and succour, or a healing for the space of three days and three nights, so that he might then employ his strength on his enemies. What Cethern son of Fintan chose was a healing for the space of three days and three nights, to the end that he might then vent his anger and strength on his enemies. For what he said was, that there would not be found after him any one he would rather have vindicate or avenge him than himself. Thereupon Fingin the prophetic physician asked of Cuchulain a vat of marrow wherewith to heal and to cure Cethern son of Fintan. Cuchulain proceeded to the camp and entrenchment of the men of Erin, and whatsoever he found of herds and flocks and droves there he took away with him. And he made a marrow-mesh of their flesh and their bones and their skins; and Cethern son of Fintan was placed in the marrow-bath till the end of three days and three nights. And his flesh began to drink in the marrow-bath about him and the marrow-bath entered in within his stabs and his cuts, his sores and his many wounds. Thereafter he arose from the marrow-bath at the end of three days and three nights. It was thus Cethern arose, with a slab of the chariot pressed to his belly so that his entrails and bowels would not drop out of him.

Arái sein barroega Fingin Fathliaig a roga do Chetharn mac Fintain, sergleghi fada fair & fortachtt & forithin d'fagbail assa athli, na dergleges teóra lá & teora n-aidchi, go n-imre féin a nert for a námtib. Is ed ón barróega Cethern mac Fintain, dergleges téora lá & teora n-aidchi, go n-imred fein a nert for a námtib, dáig issed ra ráidestar-som, na faigbed dá éis nech bud ferr leis dá athe nó da dígail andás badessin. Is and-sin conattacht Fingin Fathliaig smirammair for Coinculaind do ícc & do leigess Chethirn meic Fintain. Tanic smirammair díb eter feóil & chnámaib & lethar, acus tucad Cethern mac Fintain sin smirammair, co cend teora lá & teora n-aidche. Acus ra gab ac ól na smiramrach imme. Acus ra luid in smirammair and eter a chnedaib & eter a chrechtaib, dar a áltaib & dar a ilgonaib. And-sin atracht-som assin Cuchulaind reme i n-dúnud & illongphort fer n-hErend, & na fúair d'almaib & d'éitib & d'indilib and, tuc leis ass íat. Acus dogní smiramair i cind teora lá & teora n-aidche. Acus issamlaid attracht & clár a charpait re broind, ar ná tuitted a fobach & a inathar ass.

The outcome here described is the first published result of an experiment of bone marrow derived ex vivo expanded MSC in the presence of fetal calf serum to induce tissue repair (albeit only temporarily)!

Abbreviations

"I can believe anything, provided that it is quite incredible"

- Oscar Wilde (1854-1900)

The Picture of Doran Gray, 1891

Abbreviations

AID	Autoimmune disease
ALL	Acute lymphoblastic leukemia
ALWP	Acute Leukemia Working Party
AML	Acute myeloid leukemia
ANLL	Acute non-lymphoblastic leukemia
APC	Antigen presenting cell
ATG	Anti-thymocyte globulin
AdV	Adenovirus
BM	Bone marrow
CCMO	Centrale Commissie Mensgebonden Onderzoek
CD	Cluster determinant
CFU-F	Colony forming unit fibroblast
CFU-G (M)	Colony forming unit granulocyte (macrophage)
CME	Commissie Medische Ethiek
CML	Chronic myeloid leukemia
CMV	Cytomegalovirus
CR	Complete remission
CSA	Cyclosporine A
CST	Center for Stem Cell Therapy
CTLp	Cytotoxic T lymphocyte precursor
(m)(p)DC	(monocytoid) (plasmacytiod) Dendritic cell
DFS	Disease free survival
DLI's	Donor lymphocyte infusions
EBMT	European Group for Blood and Marrow Transplantation
EBV	Epstein Barr virus
EFS	Event free survival

FAB	French American British classification
GCP	Good clinical practice
G(M)-CSF	Granulocyte (-macrophage) colony stimulating factor
GMP	Good manufacturing practice
(a)GvHD (acute)	Graft versus host disease
GvL	Graft versus leukemia
HIV	Human immune deficiency virus
HLA	Human leukocyte antigen
(H)PBSCT	(Hemopoietic) peripheral blood stem cell transplantation
HPC	Hematopoietic progenitor cells
HSCT	Hematopoietic stem cell transplantation
IBD	Inflammatory bowel disease
IDO	Indoleamine 2, 3-dioxygenase
IHOBA	Sub-section: Immunology, hemato-oncology, bone marrow transplantation and autoimmune disease
IL	Inerleukin
INF	Interferon
IRD	Identical related donor
i.v. / I.V.	Intravenous (ly)
JMML	Juvenile myelomonocytic leukemia
LTC	Long-term cultures
LUMC	Leiden University Medical Center
MDS	Myelodysplastic syndrome
MEC	Medical ethical committee
MHC	Major histocompatibility complex
MLC	Mixed lymphocyte culture
MLR	Mixed lymphocyte reaction
MMF	Myclofenolate mofetil

MNC's	Mononuclear cells
(h)MSCs	Human mesenchymal stem (stromal) cells
MTX	Methotrexate
MUD	Matched unrelated donor
NC	Nucleated cells
NDMP	National donor marrow transplant program
NK	Natural killer
OS	Overall survival
PDWP	Pediatric Disease Working Party
PBMC	Peripheral blood mononuclear cells
PBSC	Peripheral blood stem cells
PCR	Polymerase chain reaction
SAA	Severe aplastic anemia
s.c.	Subcutaneously
(H)SCT	(Hematopoietic) Stem cell transplantation
SOP	Standard operating procedure
TGF	Tissue growth factor
Tregs	Regulatory T cells
TNF	Tissue necrosis factor
TRM	Transplant related mortality
UCB	Umbilical cord blood
UCBT	Umbilical cord blood transplant
UPN	Unique patient number
URD	Unrelated donor
WBC	White blood cell
WHO	World Health Organization