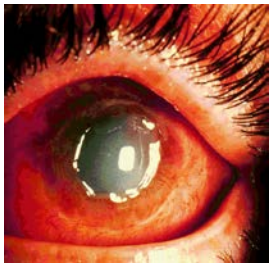
Manufacturing of Cell Therapies

(A class of regenerative medicines)

Manufacturing for an emerging industry

David J Williams

Loughborough University



Regenerative Medicine

- Replaces or regenerates human cells, tissues or organs to restore or establish normal function. *Mason and Dunhill, 2008*
- Allogeneic (all); Autologous (self); Xeno (animal)
- Opportunities for new medicine, new markets, new businesses, new jobs…. and for new manufacturing
- Health, Wealth and Quality of Life

Early Experiences in Regen Medicine

- Product usually worked clinically (*although not always as intended!*), but…
  - Process methods and regulations were poorly understood
  - Cost of manufacture often much greater than achievable sales price
  - Shipping logistics - major problem and cost
  - Inexperienced production staff and a lack of a multidisciplinary team
  - Lack of effective manufacturing was a **key** critical factor

Capable automated stem cell culture

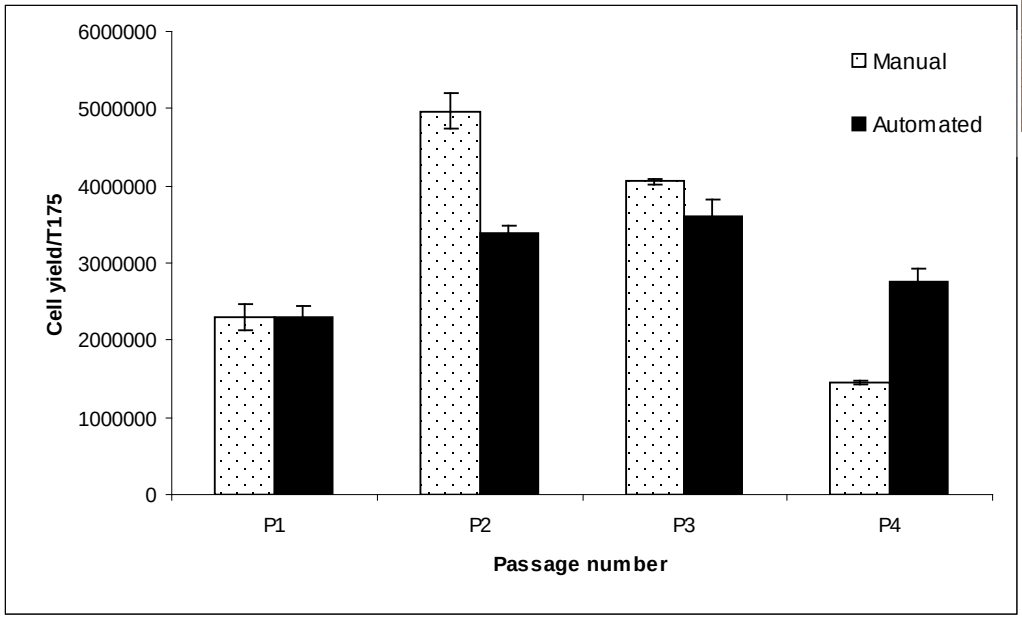
- Completely automated solution
  - Control
  - Programmable
  - Scalable
- Existing technology/ low risk process transfer
- Regulated production heritage

ORIGINAL RESEARCH

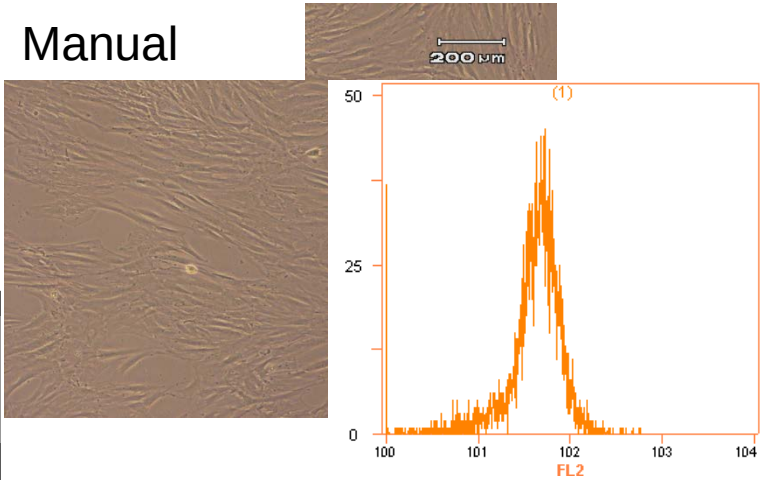
Cytotechnology (2007) 55:31–39
DOI 10.1007/s10616-007-9091-2

Manufacture of a human mesenchymal stem cell population using an automated cell culture platform

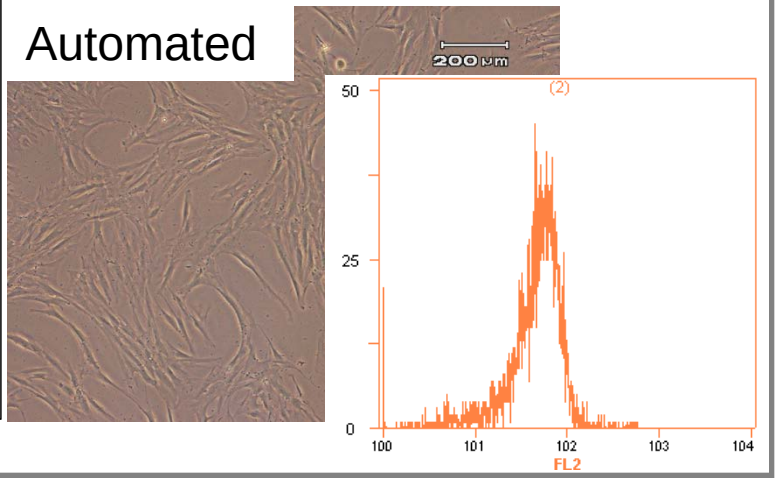
Robert James Thomas · Amit Chandra · Yang Liu · Paul C. Hourd · Paul P. Conway · David J. Williams



Manual



Automated

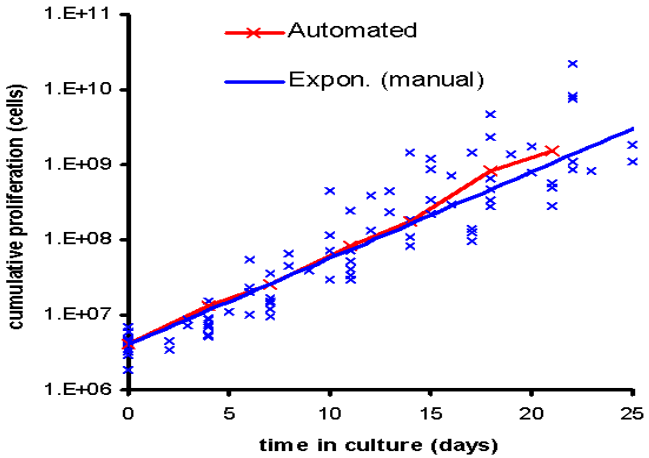


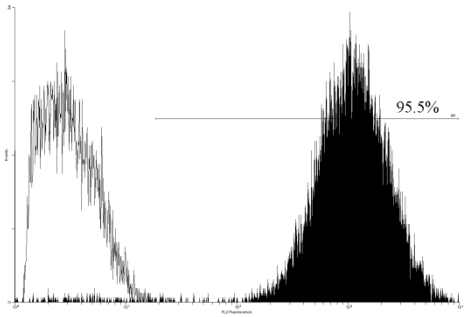
ORIGINAL RESEARCH PAPER

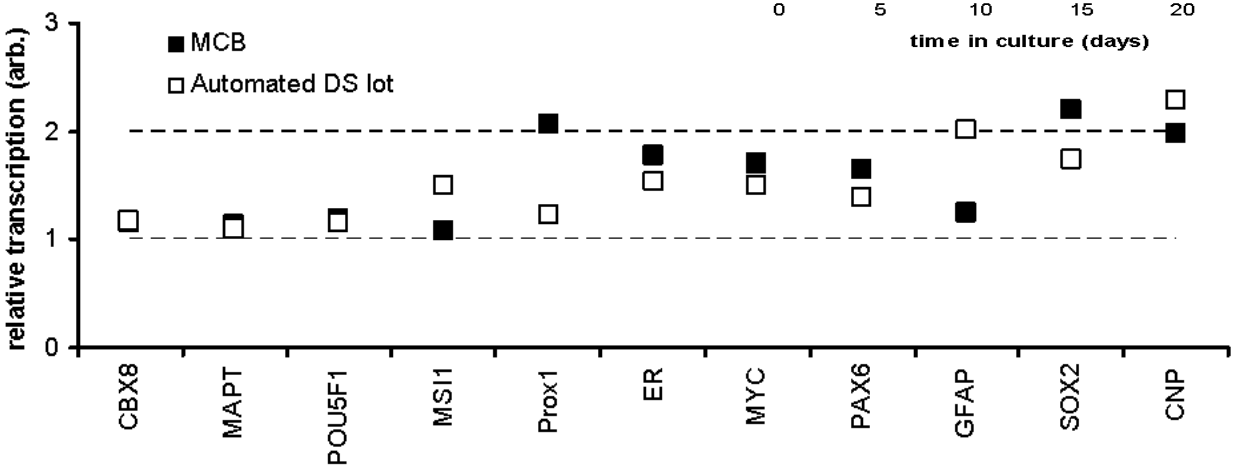
Biotechnol Lett
DOI 10.1007/s10529-009-9989-1

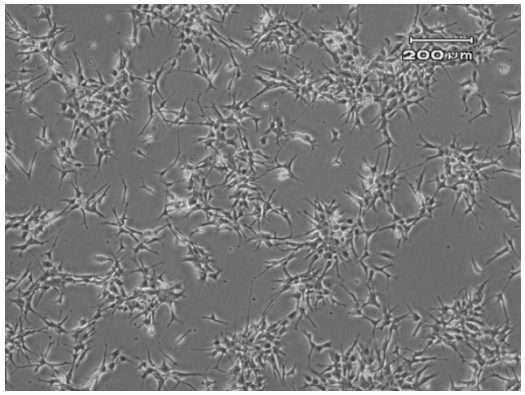
Automated, serum-free production of CTX0E03: a therapeutic clinical grade human neural stem cell line

R. J. Thomas · A. D. Hope · P. Hourd · M. Baradez · E. A. Miljan · J. D. Sinden D. J. Williams







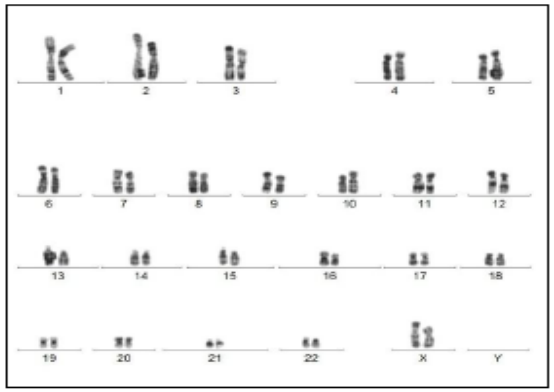


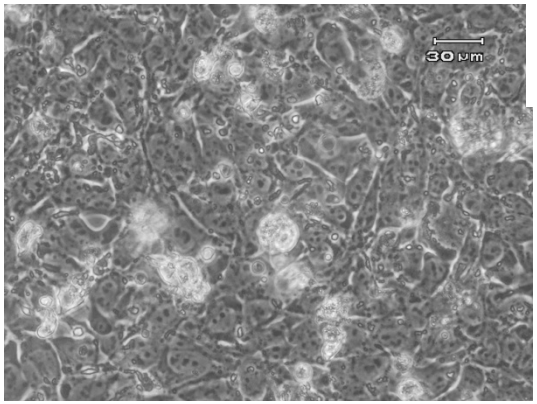
ARTICLE

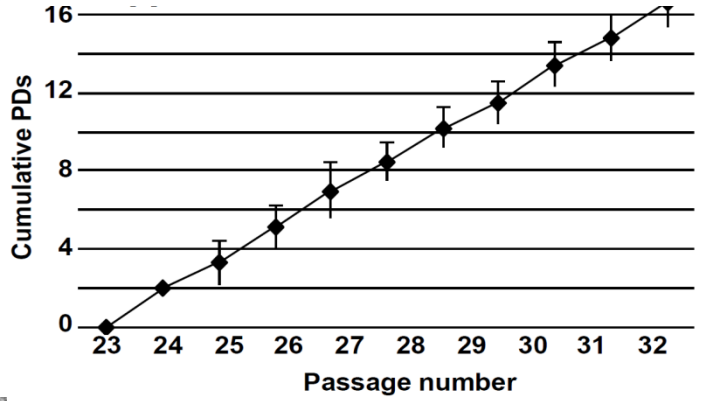
BIOTECHNOLOGY and BIOENGINEERING

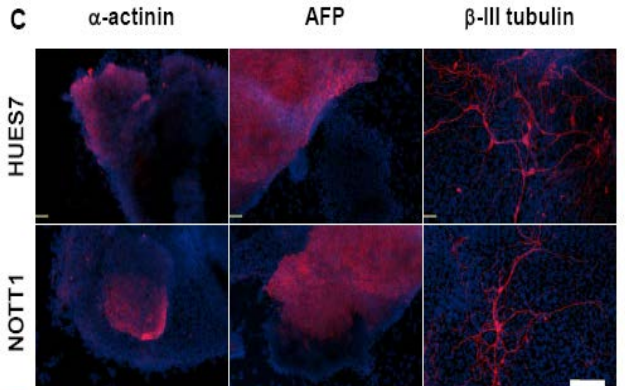
Automated, Scalable Culture of Human Embryonic Stem Cells in Feeder-Free Conditions

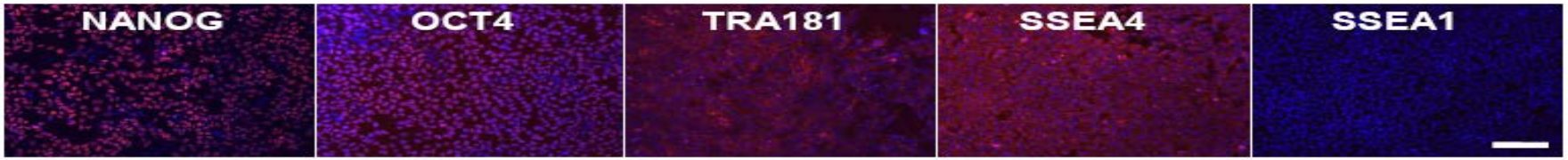
Rob J. Thomas,[1] David Anderson,[2] Amit Chandra,[1] Nigel M. Smith,[3] Lorraine E. Young,[2] David Williams,[1] Chris Denning[2]

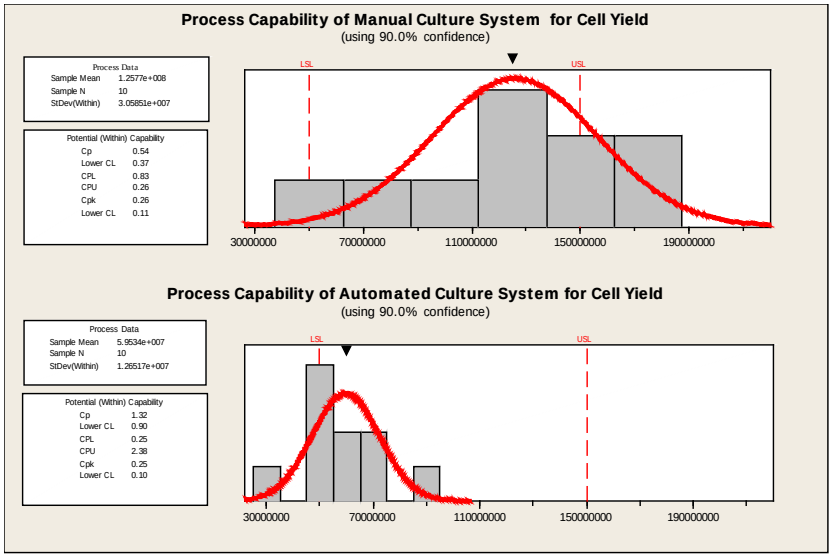












JOURNAL OF TISSUE ENGINEERING AND REGENERATIVE MEDICINE
J Tissue Eng Regen Med 2010; 4: 45–54.

Human cell culture process capability: a comparison of manual and automated production

Yang Liu, Paul Hourd, Amit Chandra and David J. Williams*
Wolfson School of Manufacturing and Mechanical Engineering, Loughborough University, Leicestershire LE11 3TU, UK

Culture System	Potential Capability	Actual Capability	Process Performance	Process Location (mean)	Process Variability	Improvement Intervention	Process Improvement compared to Manual System	
							Order of magnitude	% Defects
Manual	Cp = 0.55	Cpk = 0.26	Not capable	Centred	Poor	Reduce variability	-	21%
Automated	Cp = 1.32	Cpk = 0.25	Adequate capability	Off-centre	Good	Adjust process location	0	23%
Automated potential (centred mean)	Cp = 1.32	Cpk = 1.32	Good capability	Centred	Good	None	3	< 0.01%

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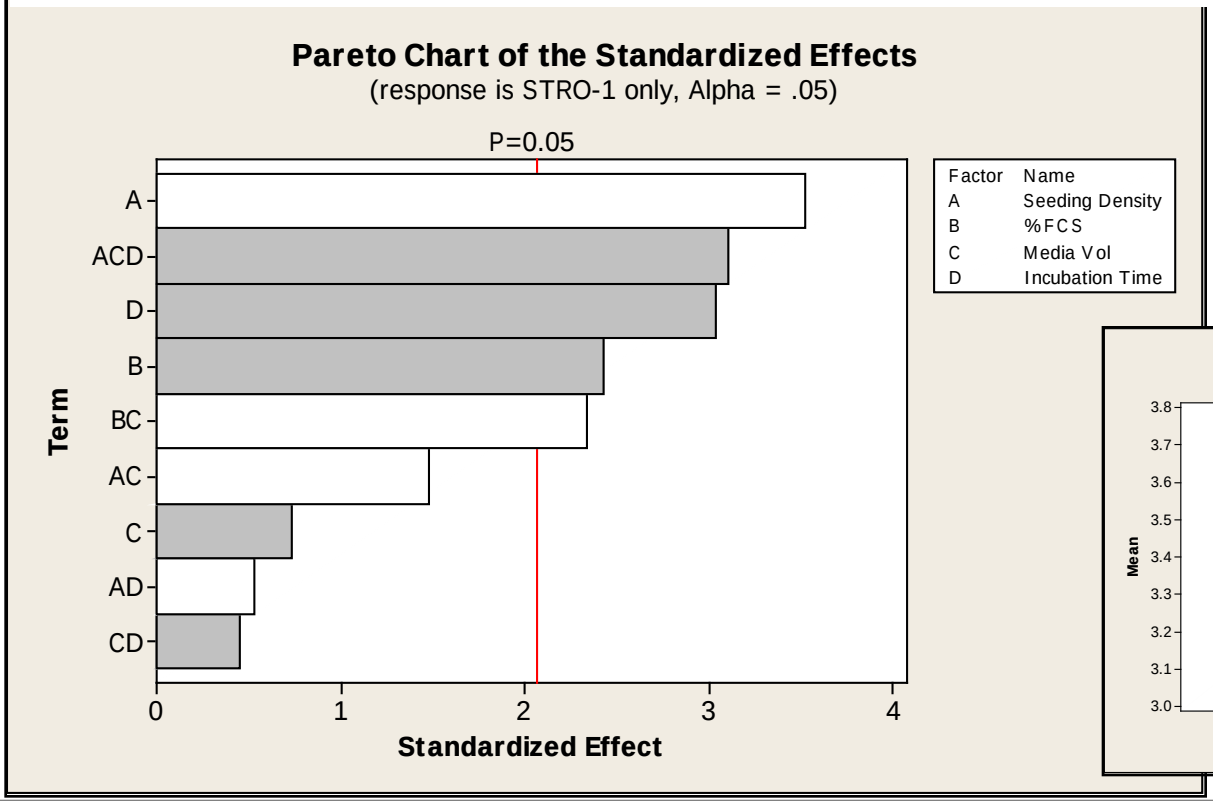
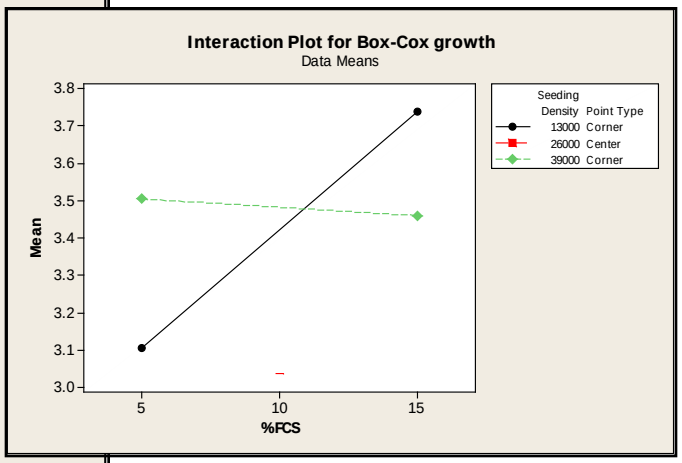
136 (2008) 148–155

Application of process quality engineering techniques to improve the understanding of the in vitro processing of stem cells for therapeutic use

R.J. Thomas*, P.C. Hourd, D.J. Williams





Where are we now?

- Some pioneers are now profitable
  - Shire ABH
  - Organogenesis
- Product regulatory environment clearer
  - Tigenix pathfinders in Europe
- Big pharma/med tech is exploring
  - Pfizer, GSK, J&J
- New cell types reduce ethical issues
  - Induced pluripotency stem cells
- A supply chain is emerging
  - CRO's, CMO's, Automation suppliers, Media
- Wins are clearer
  - Heamatological malignancies, opthalmology, musculoskeletal, blood
- Manufacturing technology for living products is emerging...
  - Teams bridging biology, engineering and the clinic

Key manufacturing research requirements

- Scaleable business models and manufacturing and supply strategies; Adoption and reimbursement paths
- Cost effective platform manufacturing technologies
  - Product specification, characterisation, processing, banking and allowable and achieveable variation
- Regulatory science that permits scaleable amortization of the regulatory and capital burden by producers
- Near patient cell processing solutions for cell therapies that require more than minimal manipulation (expansion)
- Logistics and cold chain management, cryopreservation
- Physiologically informed 3D culture