

Overview of Key Alvetex® Publications

Date: July 2011

Title: Rat Primary Hepatocytes Show Enhanced Performance and Sensitivity to Acetaminophen During Three-Dimensional Culture on a Polystyrene Scaffold Designed for Routine Use

Author: Maaïke Schutte, Bridget Fox, Marc-Olivier Baradez, Alison Devonshire, Jesus Minguez, Maria Bokhari, Stefan Przyborski, and Damian Marshall

Journal: ASSAY and Drug Development Technologies, 2011, doi: 10.1089/adt.2011.0371

Overview: Growth and function of primary rat hepatocytes was assessed on 2D and 3D polystyrene substrates. Cells grown on alvetex scaffolds exhibit a natural 3D structure, enhanced induction of metabolic enzyme expression, and differential response to expression of genes associated with phase I, II, and III drug metabolism compared with monolayer culture.

Highlights:

- Alvetex provides a solution for routine 3D culture of primary hepatocytes
- The viability of primary hepatocytes is significantly enhanced when grown on alvetex
- Induced expression of cytochrome p450 expression is radically increased in 3D culture
- Primary hepatocytes show greater sensitivity to cytotoxin when grown on alvetex
- Gene expression profiling of metabolism and transporter genes recorded in 3D culture
- Opportunity for routine 3D culture of primary hepatocytes reviewed

Title: Adipose tissue-derived stem cells display a proangiogenic phenotype on 3D scaffolds

Author: Evgenios A. Neofytou, Edwin Chang, Bhagat Patlola, Lydia-Marie Joubert, Jayakumar Rajadas, Sanjiv S. Gambhir, Zhen Cheng, Robert C. Robbins, Ramin E. Beygui

Journal: Journal of Biomedical Materials Research Part A, 2011, doi: 10.1002/jbm.a.33113

Overview: Co-culturing ASCs with endothelial cells in a 3D matrix environment enabled the generation of pre-vascularized tissue-engineered constructs, potentially surpassing the tissue thickness limitations faced by the tissue engineering community today.

Highlights:

- Demonstration of co-culture and interaction of different cell types in 3D alvetex model
- Extensive analysis of 3D culture model using a variety of alternative methods, including fluorescence imaging, confocal, scanning electron microscopy and biochemical assays
- Clear evidence of enhanced biological responses in 3D alvetex culture

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Title: Dysregulated TRK signalling is a therapeutic target in CYLD defective tumours

Author: N Rajan, R Elliott, O Clewes, A Mackay, JS Reis-Filho, J Burn, J Langtry, M Sieber-Blum, CJ Lord and A Ashworth

Journal: Oncogene, 2011, doi:10.1038/onc.2011.133

Overview: Analysis of the *CYLD* mutant tumours showed involvement of tropomyosin kinase (TRK). In vitro models including 3D primary cell cultures established from *CYLD* mutant tumours, demonstrated the function of TRK in reducing cell proliferation in cylindroma tumours.

Highlights:

- Use of alvetex to support 3D culture of primary cells from cylindroma tumours
 - Long term 3D culture was performed for 28 days followed by drug treatments
 - 3D cultures were analysed using immunoblotting and histological techniques
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Title: Validation of reference gene stability for APAP hepatotoxicity studies in different in vitro systems and identification of novel potential toxicity biomarkers

Author: Bridget C. Fox, Alison S. Devonshire, Maaïke E. Schutte, Carole A. Foy, Jesus Minguez, Stefan Przyborski, Daniel Maltman, Maria Bokhari, Damian Marshall

Journal: In Vitro Toxicology, 2011, doi: 10.1016/j.tiv.2010.08.007

Overview: Detailed analysis of reference gene expression using real time PCR in hepatocytes grown in 2D and 3D culture was used to identify novel target genes as potential markers of cellular toxicity in response to acetaminophen.

Highlights:

- Alvetex supports the growth of both HepG2 and primary hepatocytes
 - Extraction method produces sufficient yield of high quality RNA isolated from 3D cultures
 - Real time PCR used to monitor gene expression levels in 2D and 3D culture systems
 - Expression profiling of many reference genes consistent between alternative models
 - Reference genes identified as potential biomarkers of acetaminophen toxicity
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Title: Developments in three-dimensional cell culture technology aimed at improving the accuracy of in vitro analyses.

Author: Daniel J. Maltman, Stefan A. Przyborski

Journal: Biochemical Society Transactions, 2010, volume 38(4), pp1072-1075

Overview: Review contextualising the requirement for routine 3D cell culture technology

Highlights:

- Limitations of alternative materials/products
 - Introduction of alvetex and key benefits
 - Illustrative examples of liver and stem cell growth in alvetex
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Title: Emulsion-templated porous polymers as scaffolds for three dimensional cell culture: effect of synthesis parameters on scaffold formation and homogeneity

Author: Maria Bokhari, Ross J. Carnachan, Stefan A. Przyborski, Neil R. Cameron

Journal: Journal of Materials Chemistry, 2007, volume 17, pp4088-4094

Overview: Development of emulsion templated porous polymers based on polystyrene for use in 3D cell culture. Research and prototyping ultimately lead to the development of alvetex technology.

Highlights:

- In-depth evaluation of synthesis parameters on scaffold formation and homogeneity
 - Preparation of scaffolds for 3D cell culture
 - Early demonstration of technology used for 3D cell culture and growth of MG63 osteoblasts
 - Evidence of enhanced bone formation in 3D cultures compared to conventional 2D systems
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Title: Culture of HepG2 liver cells on three dimensional polystyrene scaffolds enhances cell structure and function during toxicological challenge

Author: Maria Bokhari, Ross J. Carnachan, Neil R. Cameron, Stefan A. Przyborski

Journal: Journal of Anatomy, 2007, volume 211, pp567-576

Overview: Growth of HepG2 liver cells in 3D environment enhances their cell structure and function, producing more morphological features of mammalian liver tissue

Highlights:

- Liver cultures in 3D were more heterogenous in nature compared to 2D counterparts
 - Evidence for development of hepatic structures in alvetex
 - Improved viability and albumin secretion, and reduced cell damage in alvetex vs 2D
 - Cells show enhanced resistance to MTX induced cellular toxicity in alvetex
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Title: Novel cell culture device enabling three-dimensional cell growth and improved cell function

Author: Maria Bokhari, Ross J. Carnachan, Neil R. Cameron, Stefan A. Przyborski

Journal: Biochemical and Biophysical Research Communications, 2007, volume 354, pp1095–1100

Overview: First publication dedicated to description of alvetex prototypes to support 3D cell culture using model hepatocyte cell line HepG2.

Highlights:

- Cells cultured in alvetex showed improved HepG2 culture homogeneity
 - Evidence for development of hepatic structures in alvetex
 - Increased metabolic activity and albumin secretion by HepG2 grown in alvetex
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Title: Tailoring the morphology of emulsion-templated porous polymers

Author: Ross J. Carnachan, Maria Bokhari, Stefan A. Przyborski, Neil R. Cameron

Journal: Soft Matter, 2006, volume 2, pp608-616

Overview: Detailed description of the research into the process by which porous polystyrene scaffolds are made, including a review of the different factors that influence the structure and porosity of the material.

Highlights:

- Description of High Internal Phase Emulsions (HIPE) as a method to produce porous material
 - Evidence showing how chemical and physical factors influence the formation of polyHIPE
 - Development of polyHIPE technology to create tailored materials for specific applications
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Title: Enhanced neurite outgrowth by human neurons grown on solid three-dimensional scaffolds

Author: M.W. Hayman, K.H. Smith, N.R. Cameron, S.A. Przyborski'

Journal: Biochemical and Biophysical Research Communications, 2004, volume 314, pp483–488

Overview: Original proof of concept study using early stage prototype polystyrene scaffolds to demonstrate their ability to support the growth of cells during culture.

Highlights:

- Growth of human stem cell derived neurons on early stage polystyrene scaffolds
 - Use of environmental scanning electron microscopy to visualise cells
 - Extraction of total protein from 3D cultures and subsequent immunoblotting to monitor the expression of neural markers.
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Title: Growth of human stem cell-derived neurons on solid three-dimensional polymers

Author: M.W. Hayman, K.H. Smith, N.R. Cameron, S.A. Przyborski

Journal: Journal of Biochemical and Biophysical Methods, 2004, volume 62, pp231-240

Overview: Original proof of concept study using early stage prototype polystyrene scaffolds to demonstrate their ability to support the growth of cells during culture.

Highlights:

- Growth of human stem cell derived neurons on early stage polystyrene scaffolds
 - Use of environmental scanning electron microscopy to visualise cells
 - Development of methods to coat scaffolds with poly-D-lysine and laminin
 - Evidence showing coated scaffolds promote enhanced cellular differentiation in 3D culture
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