OptiPrep™ Mini-Review MC05

Purification of pancreatic islets – a bibliography

The reference list has been divided alphabetically into the **mammalian source** of the islets:

Canine see p1; human, see pp1-7; murine see pp7-9; porcine see pp9-14; primate (non-human) see pp14; rat see pp14-16

Each of these sections is divided further into **research topic groups**. References are listed alphabetically within each section according to first author and in cases of multiple entries, are listed chronologically. **A list of review articles is provided on pp16-17.**

- A description of the original methodology using a discontinuous iodixanol gradient in a centrifuge tube is given in **Application Sheet C15**. The method has been widely adapted to use of the COBE 2991 rotor, in which both continuous and discontinuous gradients have been used.

Canine

Harrington, S., Williams, S.J., Otte, V., Barchman, S., Jones, C., Ramachandran, K. and Stehno-Bittel, L. (2017) *Improved yield of canine islet isolation from deceased donors* BMC Vet. Res., **13**: 264

Human

Chronic pancreatitis

Bellin, M.D., Freeman, M.L., Schwarzenberg, S.J., Dunn, T.B., Beilman, G.J., Vickers, S.M., Chinnakotla, S., Balamurugan, A.N. et al (2011) *Quality of life improves for pediatric patients after total pancreatectomy and islet autotransplant for chronic pancreatitis* Clin. Gastroenterol. Hepatol., **9**, 793–799

Matsumoto, S., Takita, M., Shimoda, M., Sugimoto, K., Itoh, T., Chujo, D., SoRelle, J.A., Tamura, Y. et al (2012) *Impact of tissue volume and purification on clinical autologous islet transplantation for the treatment of chronic pancreatitis* Cell Transplant., **21**, 625–632

Balamurugan, A., Loganathan, G., Tweed, B., Tucker, W., Mokshagundam, S., Williams, S. and Hughes, M. (2016) *Isolating high islet mass even from alcoholic pancreatitis pancreases intended for clinical islet auto-transplantation: improved strategies to human islet isolation technique* Am. J. Transplant., **16(S3)**, abstr 81

Continuous gradients in bottles (large scale)

Shimoda, M., Itoh, T., Iwahashi, S., Takita, M., Sugimoto, K., Kanak, M.A., Chujo, D., Naziruddin, B., Levy, M.F., Grayburn, P.A. and Matsumoto, S. (2012) *An effective purification method using large bottles for human pancreatic islet isolation* Islets **4**: 6

Encapsulation

Baron, M., Veres, A., Wolock, S.L., Faust, A.L., Gaujoux, R., Vetere, A., Ryu, J.H., Wagner, B.K. et al (2016) *A single-cell transcriptomic map of the human and mouse pancreas reveals inter- and intra-cell population structure* Cell Systems **3**, 346–360

Enck, K., McQuilling, J.P., Orlando, G., Tamburrini, R., Sivanandane, S. and Opara, E.C. (2017) *Selective osmotic shock (SOS)-based islet isolation for microencapsulation* In Methods Mol. Biol., **1479**, Cell Microencapsulation: Methods and Protocols (ed. Opara, E.C.) Springer Science+Business Media, LLC pp 191-198

Exosome production

Hasilo, C.P., Negi, S., Allaeys, I., Cloutier, N., Rutman, A.K., Gasparrini, M., Bonneil, E., Thibault, P., Boilard, E. and Paraskevas, S. (2017) *Presence of diabetes autoantigens in extracellular vesicles derived from human islets* Sci. Rep., **7**, 5000

Extracellular matrix attachment

Peloso, A., Urbani, L., Cravedi, P., Katari, R., Maghsoudlou, P., Alvarez Fallas, M.E., Sordi, V., Citro, A. et al (2016) *The human pancreas as a source of protolerogenic extracellular matrix scaffold for a new-generation bioartificial endocrine pancreas* Ann. Surg., **264**, 169–179

Gene delivery

Cheng, K., Fraga, D., Zhang, C., Kotb, M., Gaber, A.O., Guntaka, R.V. and Mahato, R.I. (2004) *Adenovirus-based vascular endothelial growth factor gene delivery to human pancreatic islets* Gene Ther., **11**, 1105-1116
Mahato, R.I., Henry, J., Narang, A.S., Sabek, O., Fraga, D., Kotb, M. and Gaber, A.O. (2003) *Cationic lipid and polymer based gene delivery to human pancreatic cells* Mol. Ther., **7**, 89-100
Narang, A.S., Cheng, K., Henry, J., Zhang, C., Sabek, O., Fraga, D., Kotb, M., Gaber, O. and Mahato, R.I. (2004) *Vascular endothelial growth factor gene delivery for revascularization in transplanted human islets* Pharmaceut. Res., **21**, 15-25

Large scale multi-site production

Ricordi, C., Goldstein, J.S., . Balamurugan, A.M., Szot, G.L., Kin, T., Liu, C., Czarniecki, C.W., Barbaro, B., Bridges, N.D. et al (2016) *National Institutes of Health–sponsored clinical islet transplantation consortium phase 3 trial: manufacture of a complex cellular product at eight processing facilities* Diabetes, **65**, 3418–3428

N-glycan profiles

Miyagawa, S., Maeda, A., Kawamura, T., Ueno, T., Usui, N., Kondo, S., Matsumoto, S., Okitsu, T., Goto, M. and Nagashima, H. (2014) *A comparison of the main structures of N-glycans of porcine islets with those from humans* Glycobiology, **24**, 125−138

Progenitor cells

Lee, S., Lee, C.M. and Kim, S.C. (2016) *Adult human pancreas-derived cells expressing stage-specific embryonic antigen 4 differentiate into Sox9-expressing and Ngn3-expressing pancreatic ducts in vivo* Stem Cell Res. Ther., **7**: 162

Transcription regulation

Lawrence, M.C., McGlynn, K., Shao, C., Duan, L., Naziruddin, B., Levy, M.F. and Cobb, M.H. (2008) *Chromatin-bound mitogen-activated protein kinases transmit dynamic signals in transcription complexes in β-cells* Proc. Natl. Acad. Sci. USA., **105**, 13315-13320

Transplantation

Allotransplant and autotransplant recipients

Bellin, M.D., Sutherland, D.E.R., Beilman, G.J., Hong-McAtee, I., Balamurugan, A.N., Hering, B.J. and Moran, A. (2011) *Similar islet function in islet allotransplant and autotransplant recipients, despite lower islet mass in autotransplants* Transplantation, **91**, 367–372

Anti-inflammatory strategy

Mita, A., Ricordi, C., Messinger, S., Miki, A., Misawa, R., Barker, S., Molano, R.D., Haertter, R. et al (2010) *Antipro-inflammatory effects of iodixanol (OptiPrep)-based density gradient purification on human islet preparations* Cell Transplant., **19**, 1537–1546
Takita, M., Matsumoto, S., Shimoda, M., Chujo, D., Itoh, T., SoRelle, J.A., Purcell, K., Onaca, N., Naziruddin, B. and Levy. M.F. (2012) *Safety and tolerability of the T-cell depletion protocol coupled with anakinra and etanercept for clinical islet cell transplantation* Clin. Transplant., **26**, E471–E484

Clinical problems

Naziruddin, B., Iwahashi, S., Kanak, M.A., Takita, M., Itoh, T. and Levy, M.F. (2014) *Evidence for instant blood-mediated inflammatory reaction in clinical autologous islet transplantation* Am. J. Transplant., 1**4**, 428–437
Takita, M., Matsumoto, S., Noguchi, H., Shimoda, M., Ikemoto, T., Chujo, D., Tamura, Y., Olsen, G.S. et al (2012) *Adverse events in clinical islet transplantation: one institutional experience* Cell Transplant., **21**, 547–551
Wang, L-j., Young, S., Misawa, R., Azzam, R., Wang, X., Gołąb, K., Cochet, O., Savari, O., Tibudan, M. et al (2014) *Chronic pancreatitis and primary sclerosing cholangitis—first report of intrahepatic autologous islet tansplantation* J. Gastrointest. Surg., **18**, 845−850

Collagenase effects

Balamurugan, A.N., Breite, A.G., Anazawa, T., Loganathan, G., Wilhelm, J.J., Papas, K.K., Dwulet, F.E., McCarthy, R.C. and Hering, B.J. (2010) *Successful human islet isolation and transplantation indicating the importance of class 1 collagenase and collagen degradation activity assay* Transplantation**, 89**, 954–961

Culture effects and islet function

Gaber, A. O., Fraga, D.W., Callicutt, C.S., Gerling, I.C., Sabek, O.M. and Kotb, M.Y. (2001) *Improved in vivo pancreatic iselt function after prolonged in vitro islet culture* Transplantation, **72**, 1730-1736

Hering, B.J., Kandaswamy, R., Harmon, J.V., Ansite, J.D., Clemmings, S.M., Sakai, T., Paraskevas, S., Eckman, P.M. et al (2004) *Transplantation of cultured islets from two-layer preserved pancreases in type 1 diabetes with anti-CD3 antibody* Am. J. Transplant., **4**, 390-401

Noguchi, H., Naziruddin, B., Jackson, A., Shimoda, M., Ikemoto, T., Fujita, Y., Chujo, D., Takita, M. et al (2010) *Low-temperature preservation of isolated islets is superior to conventional islet culture before islet transplantation* Transplantation, **89**, 47-54

Noguchi, H., Naziruddin, B., Jackson, A., Shimoda, M., Ikemoto, T., Fujita, Y., Chujo, D., Takita, M. et al (2012) *Fresh islets are more effective for islet transplantation than cultured islets* Cell Transplant., **21**, 517–523

Rush, B.T., Fraga, D.W., Kotb, M.Y., Sabek, O.M., Lo, A., Gaber, L.W., Halim, A-B. and Gaber, A.A. (2004) *Preservation of human pancreatic islet in vivo function after 6-month culture in serum-free media* Transplantation, **77**, 1147-1154

Donor pancreas optimization

Matsumoto, S., Noguchi, H., Takita, M., Shimoda, M., Tamura, Y., Olsen, G., Naziruddin, B., Onaca, N. and Levy, M.F. (2010) *ET-Kyoto ductal injection and density-adjusted purification combined with potent anti-inflammatory strategy facilitated single-donor islet transplantation: case reports* Transplant. Proc., **42**, 2159–2161

Noguchi, H. and Matsumoto, S. (2008) *Islet transplantation at the Diabetes Research Institute Japan* J. Hepatobiliary Pancreat. Surg., **15**, 278-283

Noguchi, H., Naziruddin, B., Jackson, A., Shimoda, M., Ikemoto, T., Fujita, Y., Chujo, D., Takita, M. et al (2010) *Low-temperature preservation of isolated islets is superior to conventional islet culture before islet transplantation* Transplantation, **89**, 47-54

Donor selection (living)

Noguchi, H. and Matsumoto, S. (2008) *Islet transplantation at the Diabetes Research Institute Japan* J. Hepatobiliary Pancreat. Surg., **15**, 278-283

Donor selection (marginal cadaver)

Nagata, H., Matsumoto, S., Okitsu, T., Iwanaga, Y., Noguchi, H., Yonekawa, Y., Kinukawa, T., Shimizu, T. et al (2006) *Procurement of the human pancreas for pancreatic islet transplantation from marginal cadaver donors* Transplantation, **82**, 327-331

Donor selection (non-heart beating)

Matsumoto, S. and Tanaka, K. (2005) *Pancreatic islet transplantation using non-heart-beating donors (NHBDs)* J. Hepatobiliary Pancreat. Surg., **12**, 227-230

Noguchi, H., Iwanaga, Y., Okitsu, T., Nagata, H., Yonekawa, Y. and Matsumoto, S. (2006) *Evaluation of islet transplantation from non-heart beating donors* Am. J. Transplant., **6**, 2476-2482

Noguchi, H. and Matsumoto, S. (2008) *Islet transplantation at the Diabetes Research Institute Japan* J. Hepatobiliary Pancreat. Surg., **15**, 278-283

Noguchi, H., Yamada, Y., Okitsu, T., Iwanaga, Y., Nagata, H., Kobayashi, N., Hayashi, S. and Matsumoto, S. (2008) *Secretory unit of islet in transplantation (SUIT) and engrafted islet rate (EIR) indexes are useful for evaluating single islet transplantation* Cell Transplant., **17,** 121-128

Okitsu, T., Matsumoto, S., Iwanaga, Y., Noguchi, H., Nagata, H., Yonekawa, Y., Maekawa, T. and Tanaka, K. (2005) *Kyoto islet isolation method: the optimized one for non-heart-beating donors with highly efficient islet retrieval* Transplant. Proc., **37**, 3391-3392

Saito, T., Gotoh, M., Satomi, S., Uemoto, S., Kenmochi, T., Itoh, T., Kuroda, Y., Yasunami, Y., Matsumoto, S. and Teraoka, S. (2010) *Islet transplantation using donors after cardiac death: report of the Japan Islet Transplantation Registry* Transplantation, **90**, 740–747

Donor selection (paediatric patients)

Bellin, M.D., Blondet, J.J., Beilman, G.J., Dunn, T.B., Balamurugan, A.N., Thomas, W., Sutherland D.E.R., Moran, A. (2010) *Predicting islet yield in pediatric patients undergoing pancreatectomy and autoislet transplantation for chronic pancreatitis* Pediatr. Diabetes, **11**, 227–234

Donor selection (review)

Kin, T. (2010) *Islet isolation for clinical transplantation* In Adv. Exp. Med. Biol., **654**, The Islets of Langerhans (ed. Islam, M.S.) Springer Science + Business Media pp. 683-710

Donor selection (single donor)

Hering, B.J., Kandaswamy, R., Ansite, J.D., Eckman, P.M., Nakano, M., Sawada, T., Matsumoto, I., Ihm, S-H. et al (2005) *Single-donor, marginal-dose islet transplantation in patients with type 1 diabetes* J. Am. Med. Assoc. 830-835

Matsumoto, S., Noguchi, H., Takita, M., Shimoda, M., Tamura, Y., Olsen, G., Naziruddin, B., Onaca, N. and Levy, M.F. (2010) *ET-Kyoto ductal injection and density-adjusted purification combined with potent anti-inflammatory strategy facilitated single-donor islet transplantation: case reports* Transplant. Proc., **42**, 2159–2161

Immunosuppression of diabetic patient

Bellin, M.D., Kandaswamy, R., Parkey, J., Zhang, H-J., Liu, B., Ihm, S.H., Ansite, J.D., Witson, J. et al (2008) *Prolonged insulin independence after islet allotransplants in recipients with type 1 diabetes* Am. J. Transplant., **8**, 2463-2470

Hering, B.J., Kandaswamy, R., Ansite, J.D., Fckman, P.M., Nakano, M., Sawada, T., Matsumoto, I., Ihm, S-H., Zhang, H-J., Hunter, D.W. and Sutherland, D.E.R. (2003) *Successful single donor islet transplantation in type 1 diabetes* Int. Pancreas Islet Transpl. Assoc., Abstr. 012

Hering, B.J., Kandaswamy, R., Harmon, J.V., Ansite, J.D., Clemmings, S.M., Sakai, T., Paraskevas, S., Eckman, P.M. et al (2004) *Transplantation of cultured islets from two-layer preserved pancreases in type 1 diabetes with anti-CD3 antibody* Am. J. Transplant., **4**, 390-401

Takita, M., Matsumoto, S., Shimoda, M., Chujo, D., Itoh, T., SoRelle, J.A., Purcell, K., Onaca, N., Naziruddin, B. and Levy. M.F. (2012) *Safety and tolerability of the T-cell depletion protocol coupled with anakinra and etanercept for clinical islet cell transplantation* Clin. Transplant., **26**, E471–E484

OptiPrep – Ficoll comparison

Mita, A., Ricordi, C., Messinger, S., Miki, A., Misawa, R., Barker, S., Molano, R.D., Haertter, R. et al (2010) *Antipro-inflammatory effects of iodixanol (OptiPrep)-based density gradient purification on human islet preparations* Cell Transplant., **19**, 1537–1546

Supplemental islet transplantation

Matsumoto, S., Takita, M., Shimoda, M., Chujo, D., Itoh, T., Iwahashi, S., SoRelle, J.A., Tamura, Y. et al (2011) *Insulin independence by supplemental islet transplantation 5 years after initial islet transplantation* J. Diabetes, **3**, 353–355

Warm ischaemia

Matsumoto, S. and Tanaka, K. (2005) *Pancreatic islet transplantation using non-heart-beating donors (NHBDs)* J. Hepatobiliary Pancreat. Surg., **12**, 227-230

Nagata, H., Matsumoto, S., Okitsu, T., Iwanaga, Y., Noguchi, H., Yonekawa, Y., Kinukawa, T., Shimizu, T. et al (2006) *Procurement of the human pancreas for pancreatic islet transplantation from marginal cadaver donors* Transplantation, **82**, 327-331

Yield/viability/function

β-cell proliferation

Purwana, I., Zheng, J., Li, X., Deurloo, M., Son, D.O., Zhang, Z. et al (2014) *GABA promotes human β-cell proliferation and modulates glucose homeostasis* Diabetes, **63**, 4197–4205

Chemokine/Cytokine production

Mita, A., Ricordi, C., Miki, A., Barker, S., Khan, A., Alvarez, A., Hashikura, Y., Miyagawa, S., and Ichii, H. (2008) *The purification method using iodixanol (OptiPrep)-based density gradient significantly reduce cytokine/chemokine production from human islet preparations, leading to prolonged cell survival during culture* Transplantation **86** (Suppl. 2) 570

Mita, A., Ricordi, C., Miki, A., Barker, S., Khan, A., Alverez, A., Hashikura, Y., Miyagawa, S. and Ichii, H. (2009) *Purification method using iodixanol (OptiPrep)-based density gradient significantly reduces cytokine*

chemokine production from human islet preparations, leading to prolonged β-cell survival during pretransplantation culture Transplant. Proc., **41**, 314-315
Sabek, O.M., Fraga, D.W., Henry, J., Gaber, L.W., Kotb, M. and Gaber, A.O. (2007) *Expression of transforming growth factor-β by human islets: impact in islet viability and function* Cell Transplant., **16**, 775-785

Collagenase

Balamurugan, A.N., Green, M.L., Breite, A.G., Loganathan, G., Wilhelm, J.J., Tweed, B., Vargova, L. Lockridge, A., Kuriti, M. et al (2016) *Identifying effective enzyme activity targets for recombinant class I and class II collagenase for successful human islet isolation* Transplant. Dir., **2**, e54

Culture (short-term) and other treatments of isolated islets

Ihm, S-H., Matsumoto, I., Zhang, H.J., Ansite, J.D. and Hering, B.J. (2009) *Effect of short-term culture on functional and stress-related parameters in isolated human islets* Transplant Int., **22**, 207-216
Noguchi, H., Naziruddin, B., Jackson, A., Shimoda, M., Ikemoto, T., Fujita, Y., Chujo, D., Takita, M. et al (2010) *Low-temperature preservation of isolated islets is superior to conventional islet culture before islet transplantation* Transplantation, **89**, 47-54
Noguchi, H., Naziruddin, B., Jackson, A., Shimoda, M., Ikemoto, T., Fujita, Y., Chujo, D., Takita, M. et al (2012) *Fresh islets are more effective for islet transplantation than cultured islets* Cell Transplant., **21**, 517–523

Donor type and age, effect of

Anazawa, T., Balamurugan, A.N., Bellin, M., Zhang, H.J., Matsumoto, S., Yonekawa, Y., Tanaka, T., Loganathan, G. et al (2009) *Human islet isolation for autologous transplantation: comparison of yield and function using SERVA/Nordmark versus Roche enzymes* Am. J. Transplant., **9**, 2383–2391
Avila, J.G., Agarwal, A., Turgeon, N., Cano, J.A., Turner, A., Russell, M.C., Kirk, A.D., Pearson, T., C.P. Larsen (2009) *Identification of critical factors leading to successful islet isolations and transplantation* Am. J. Transplant., **9**, Supp 2, 406
Bellin, M.D., Blondet, J.J., Beilman, G.J., Dunn, T.B., Balamurugan, A.N., Thomas, W., Sutherland D.E.R., Moran, A. (2010) *Predicting islet yield in pediatric patients undergoing pancreatectomy and autoislet transplantation for chronic pancreatitis* Pediatr. Diabetes, **11**, 227–234
Ihm, S-H., Matsumoto, I., Sawada, T., Nakano, M., Zhang, H.J., Ansite, J.D., Sutherland, D.E.R. and Hering, B.J. (2006) *Effect of donor age on function of isolated human islets* Diabetes, **55**, 1361-1368
Matsumoto, I., Sawada, T., Nakano, M., Sakai, T., Liu, B., Ansite, J.D., Zhang, H-J., Kandaswamy, R., Sutherland, D.E.R. and Hering, B.J. (2004) *Improvement in islet yield from obese donors for human islet transplants* Transplantation, **78**, 880-885
Matsumoto, S., Okitsu, T., Iwanaga, Y., Noguchi, H., Nagata, H., Yonekawa, Y., Yamada, Y., Fukuda, K. et al (2006) *Successful islet transplantation from nonheartbeating donor pancreata using modified Ricordi islet isolation method* Transplantation **82**, 460-465

Ductal perfusion

Matsumoto, S., Noguchi, H., Takita, M., Shimoda, M., Tamura, Y., Olsen, G., Naziruddin, B., Onaca, N. and Levy, M.F. (2010) *ET-Kyoto ductal injection and density-adjusted purification combined with potent anti-inflammatory strategy facilitated single-donor islet transplantation: case reports* Transplant. Proc., **42**, 2159–2161
Matsumoto, S., Noguichi, H., Shimoda, M., Ikemoto, T., Naziruddin, B., Jackson, A., Tamura, Y., Olson, G. et al (2010) *Seven consecutive successful clinical islet isolations with pancreatic ductal injection* Cell Transplant., **19**, 291–297
Takita, M., Itoh, T., Shimoda, M., Kanak, M.A., Shahbazov, R., Kunnathodi, F., Lawrence, M.C., Naziruddin, B. and Levy, M.F. (2014) *Pancreatic ductal perfusion at organ procurement enhances islet yield in human islet isolation* Pancreas, **43**, 1249−1255

Endotoxin levels in reagents

Linetsky, E., Inverardi, L., Kenyon, N.S., Alejandro, R. and Ricordi, C. (1998) *Endotoxin contamination of reagents used during isolation and purification of human pancreatic islets* Transplant. Proc., **30**, 345-346

Enzyme digestion

Balamurugan, A.N., Loganathan, G., Bellin, M.D., Wilhelm, J.J., Harmon, J., Anazawa, T., Soltani, S.M., Radosevich, D.M. et al (2012) *A new enzyme mixture to increase the yield and transplant rate of autologous and allogeneic human islet products* Transplantation, **93**, 693–702

Functional properties of gradient isolates
Sweet, I.R., Cook, D.L., Wiseman, R.W., Greenbaum, C.J., Lernmark, A., Matsumoto, S., Teague, J.C. and Krohn, K.A. (2002) *Dynamic perifusion to maintain and assess isolated pancreatic islets* Diabetes Techn. Therapeut., **4**, 67-76

GABA, effects of
Prud'homme, G.J., Glinka, Y., Hasilo, C., Paraskevas, S., Li, X. and Wang, Q. (2013) *GABA protects human islet cells against the deleterious effects of immunosuppressive drugs and exerts immunoinhibitory effects alone* Transplantation, **96**, 616-623
Purwana, I., Zheng, J., Li, X., Deurloo, M., Son, D.O., Zhang, Z. et al (2014) *GABA promotes human β-cell proliferation and modulates glucose homeostasis* Diabetes, **63**, 4197–4205

Gradient methodology
Anazawa, T., Matsumoto, S., Yonekawa, Y., Loganathan, G., Wilhelm, J.J., Soltani, S.M., Papas, K.K., Sutherland, D.E.R., Hering, B.J. and Balamurugan, A.N. (2011) *Prediction of pancreatic tissue densities by an analytical test gradient system before purification maximizes human islet recovery for islet autotransplantation /allotransplantation* Transplantation, **91**, 508–51
Mita, A., Ricordi, C., Messinger, S., Miki, A., Misawa, R., Barker, S., Molano, R.D., Haertter, R. et al (2009) *Superiority of iodixanol (OptiPrep) over Ficoll in human islet purification* Am. J. Transplant., **9** Supp. 2, 406
Noguchi, H., Ikemoto, T., Naziruddin, B., Jackson, A., Shimoda, M., Fujita, Y., Chujo, D., Takita, M. et al (2009) *Iodixanol-controlled density gradient during islet purification improves recovery rate in human islet isolation* Transplantation, **87**, 1629–1635
Noguchi, H., Naziruddin, B., Shimoda, M., Fujita, Y., Chujo, D., Takita, M., Peng, H., Sugimoto, K. et al (2012) *Evaluation of osmolality of density gradient for human islet purification* Cell Transplant., **21**, 493–500
Van der Burg, M.P.M., Ranuncoli, A., Molano, R., Kirlew, T., Ringers, J., Bouwman, E. and Ricordi, C. (1998) *Efficacy of the novel iodixanol – UWS density gradient for human islet purification* Acta Diabetol., **35**, 247
Van der Burg, M.P.M., Ranuncoli, A., Molano, R., Kirlew, T., Ringers, J., Bouwman, E., Terpstra, O.T. and Ricordi, C. (1999) *OptiPrep for human islet purification* Cell Transplant., **8**, abstr. 57
Yonekawa, Y., Balamurugan, A.N., Matsumoto, S., Tanaka, T., Gilmore, T.R., Ansite, J.D., Zhang, H., Sutherland, D.E.R. and Hering, B.J. (2007) *The use of test gradients to determine the bottom layer density for subsequent continuous isopycnic purification of human islets on a COBE 2991 cell processor* CTS-IPITA-IXA, Minneapolis 2007 Joint Conference Abstracts, p 480

HMGB1 release levels
Itoh, T., Takita, M., SoRelle, J.A., Shimoda, M., Sugimoto, K., Chujo, D., Qin, H., Naziruddin, B., Levy, M.F. and Matsumoto, S. (2012) *Correlation of released HMGB1 levels with the degree of islet damage in mice and humans and with the outcomes of islet transplantation in mice* Cell Transplant., **21**, 1371–1381

IL-1β and TNF-α blockage
Matsumoto, S., Takita, M., Chaussabel, D., Noguchi, H., Shimoda, M., Sugimoto, K., Itoh, T., Chujo, D. et al (2011) *Improving efficacy of clinical islet transplantation with iodixanol-based islet purification, thymoglobulin induction, and blockage of IL-1β and TNF-α* Cell Transplant., **20**, 1641–1647

Metabolic assessment
Lundberg, R., Beilman, G.J., Dunn, T.B., Pruett, T.L., Chinnakotla, S.C., Radosevich, D.M., Robertson, R.P., Ptacek, P. et al (2013) *Metabolic assessment prior to total pancreatectomy and islet autotransplant: utility, limitations and potential* Am. J. Transplant., **13**, 2664–2671

Multi-centre analysis
Kaddis, J.S., Danobeitia, J.S., Niland, J.C., Stiller, T. and Fernandez, L.A. (2010) *Multicenter analysis of novel and established variables associated with successful human islet isolation outcomes* Am. J. Transplant., **10**, 646–656

Non-heart-beating cadavers
Liu, X., Matsumoto, S., Okitsu, T., Iwanaga, Y., Noguchi, H., Yonekawa, Y., Nagata, H., Kamiya, H. et al (2008) *Analysis of donor- and isolation-related variables from non-heart-beating donors (NHBDs) using the Kyoto islet isolation method* Cell Transplant., **17**, 649-656

Matsumoto, S., Okitsu, T., Iwanaga, Y., Noguchi, H., Nagata, H., Yonekawa, Y., Yamada, Y., Fukuda, K. et al (2006) *Successful islet transplantation from nonheartbeating donor pancreata using modified Ricordi islet isolation method*

Pancreas treatment and preservation prior to gradient purification

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Xenotransplantation

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Preservation of β-cell function

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Jung, K.C., Park, C-G., Jeon, Y.K., Park, H.J., Ban, Y.L., Min, H.S, Kim, E.J., Kim, J.Y. et al (2011) *In situ induction of dendritic cell–based T cell tolerance in humanized mice and nonhuman primates* J. Exp. Med., **208**, 2477-2488

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Yield/viability/function

Allograft functions

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Gradient yield and purity

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Mini-Review MC05; 4th edition, October 2017