

OptiPrep™ Mini-Review MC05

Purification of pancreatic islets – a bibliography

The reference list has been divided alphabetically into the species source of the islets ([human](#), see p1; [murine](#) see p7; [porcine](#) see p9, [primate \(non-human\)](#) see p14; [rat](#) see p14) and 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 pp15-16.](#)

- ◆ 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.
- ◆ This OptiPrep™ Application Sheet may be accessed from the Index of the “Mammalian and non-mammalian cells” file either on the OptiPrep™ Applications flash-drive or from the following website: www.axis-shield-density-gradient-media.com (click on “Methodology”).

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., Hering, B.J., Radosevich, D.M., Moran, A. and Sutherland, D.E.R. (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., Rahman, A.M., Onaca, N., Naziruddin, B. and Levy, M.F. (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

[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 prototolerogenic 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

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., Khan, A., Miyagawa, S., Pileggi, A., Inverardi, L., Alejandro, R., Hering, B.J. and Ichii, H. (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., **14**, 428–437

Takita, M., Matsumoto, S., Noguchi, H., Shimoda, M., Ikemoto, T., Chujo, D., Tamura, Y., Olsen, G.S., Naziruddin, B., Purcell, K., Onaca, N. and Levy, M.F. (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., Gołab, K., Cochet, O., Savari, O., Tibudan, M., Millis, J.M., Matthews, J.B. and Witkowski, P. (2014) *Chronic pancreatitis and primary sclerosing cholangitis—first report of intrahepatic autologous islet transplantation* 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 I 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 islet function after prolonged in vitro islet culture* Transplantation, **72**, 1730–1736

Hering, B.J., Kandaswamy, R., Harmon, J.V., Ansrite, J.D., Clemmings, S.M., Sakai, T., Paraskevas, S., Eckman, P.M., Sageshima, J., Nakano, M., Sawada, T., Matsumoto, I., Zhang, H.J., Sutherland, D.E.R. and Bluestone, J.A. (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., Kobayashi, N., Onaca, N., Levy, M.F. and Matsumoto, S. (2010) *Low-temperature preservation of isolated islets is superior to conventional islet culture before islet transplantation* Transplantation, **89**, 47–54

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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., Kobayashi, N., Onaca, N., Levy, M.F. and Matsumoto, S. (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., Miyakawa, S., Shiraki, R., Hoshinaga, K. and Tanaka, K. (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

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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., Zhang, H-J., Parkey, J., Hunter, D.W. and Sutherland, D.E.R. (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., Bansal-Pakala, P., Balamurugan, A.N., Papas, K., Sutherland, D.E.R., Moran, A. and Hering, B.J. (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., Sageshima, J., Nakano, M., Sawada, T., Matsumoto, I., Zhang, H.J., Sutherland, D.E.R. and Bluestone, J.A. (2004) *Transplantation of cultured islets from two-layer preserved pancreases in type 1 diabetes with anti-CD3 antibody* Am. J. Transplant., **4**, 390-401
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OptiPrep – Ficoll comparison

- Mita, A.**, Ricordi, C., Messinger, S., Miki, A., Misawa, R., Barker, S., Molano, R.D., Haertter, R., Khan, A., Miyagawa, S., Pileggi, A., Inverardi, L., Alejandro, R., Hering, B.J. and Ichii, H. (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., Rahman, A., Purcell, K., Naziruddin, B., Onaca, N. and Levy, M.F. (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., Miyakawa, S., Shiraki, R., Hoshinaga, K. and Tanaka, K. (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., Alvarez, 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

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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., Kobayashi, N., Onaca, N., Levy, M.F. and Matsumoto, S. (2010) *Low-temperature preservation of isolated islets is superior to conventional islet culture before islet transplantation* Transplantation, **89**, 47-54
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Donor type and age, effect of

- Anazawa, T.**, Balamurugan, A.N., Bellin, M., Zhang, H.J., Matsumoto, S., Yonekawa, Y., Tanaka, T., Loganathan, G., Papas, K.K., Beilman, G.J., Hering, B.J. and Sutherland, D.E.R/ (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
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- Matsumoto, I.**, Sawada, T., Nakano, M., Sakai, T., Liu, B., Ansrite, 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., Shibata, T., Kasai, Y., Maekawa, T., Wada, H., Nakamura, T. and Tanaka, K. (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
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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., Yuasa, T., Tiwari, M., Papas, K.K., McCarthy, R., Sutherland, D.E.R. and Hering, B.J. (2012) *A new enzyme mixture to increase the yield and transplant rate of autologous and allogeneic human islet products* Transplantation, **93**, 693–702

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GABA, effects of

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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 /allograft Transplantation*, **91**, 508–51
- Mita, A.**, Ricordi, C., Messinger, S., Miki, A., Misawa, R., Barker, S., Molano, R.D., Haertter, R., Alvarez, A., Khan, A., Pileggi, A., Miyagawa, S., Inverardi, L., Ichii, H. (2009) *Superiority of iodixanol (OptiPrep) over Ficoll in human islet purification* Am. J. Transplant., **9** Supp. 2, 406
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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-1 β and TNF- α blockage

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Metabolic assessment

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Transplantation

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Xenotransplantation

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Preservation of β-cell function

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T cell effects

Jung, K.C., Park, C-G., Jeon, Y.K., Park, H.J., Ban, Y.L., Min, H.S, Kim, E.J., Kim, J.Y., Kang, B.H., Park, S.P., Bae, Y., Yoon, I-H., Kim, Y-H., Lee, J-I., Kim, J.S., Shin, J-S., Yang, J., Kim, S.J., Rostlund, E., Muller, W.A. and Park, S.H. (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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