

OptiPrep™ Reference List RC04

Purification of pancreatic islets

References are listed according to source: canine p1; human pp1-8, murine pp8-10, porcine pp10-16, primate (non-human) p16, rat pp16-18

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 pp18-19.**

For the original methodology using a discontinuous iodixanol gradient see **Application Sheet C16**.

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

Harrington, S., Williams, J., Rawal, S., Ramachandran, K. and Stehno-Bittel, L. (2017) *Hyaluronic acid/collagen hydrogel as an alternative to alginate for long-term immunoprotected islet transplantation* Tissue Eng. Part A, **23**, 1088-1099

Human

Autoimmune response

Rutman, A.K., Negi, S., Gasparini, M., Hasilo, C.P., Tchervenkov, J., and Paraskevas, S. (2018) *Immune response to extracellular vesicles from human islets of Langerhans in patients with type 1 diabetes* Endocrinology, **159**, 3834–3847

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

Weaver, J.D., Headen, D.M., Coronel, M.M., Hunckler, M.D., Shirwan, H. and García, A.J. (2019) *Synthetic poly(ethylene glycol)-based microfluidic islet encapsulation reduces graft volume for delivery to highly vascularized and retrievable transplant site* Am J Transplant. 2019, **19**, 1315–1327

Exosome production

Hasilo, C.P., Negi, S., Allaey, 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

Rutman, A.K., Negi, S., Gasparrini, M., Hasilo, C.P., Tchervenkov, J., and Paraskevas, S. (2018) *Immune response to extracellular vesicles from human islets of Langerhans in patients with type 1 diabetes* Endocrinology, **159**, 3834–3847

Extracellular matrix attachment

Loganathan, G., Subhashree, V., Narayanan, S., Tweed, B., Goedde, M.A., Gunaratnam, B., Tucker, W.W., Goli, P. et al (2019) *Improved recovery of human islets from young donor pancreases utilizing increased protease dose to collagenase for digesting peri-islet extracellular matrix* Am. J. Transplant., **19**, 831–843

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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

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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

Pancreatectomy (complications)

Shahbazov, R., Naziruddin, B., Salam, O., Saracino, G., Levy, M.F., Beecherl, E. and Onaca, N. (2020) *The impact of surgical complications on the outcome of total pancreatectomy with islet auto-transplantation* Am. J. Surgery, **219**, 99–105

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

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Transplantation

Allotransplant and autotransplant recipients

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Autotransplantation

Saravanan, P.B., Kanak, M.A., Chang, C.A., Darden, C., Yoshimatsu G., Lawrence, M.C. and Naziruddin, B. (2018) *Islet damage during isolation as assessed by miRNAs and the correlation of miRNA levels with post-transplantation outcome in islet autotransplantation* Am. J. Transplant., **18**, 982–989

Shahbazov, R., Naziruddin, B., Yadav, K., Saracino, G., Yoshimatsu, G., Kanak, M.A., Beecher, E., Kim, P.T. and Levy, M.F. (2018) *Risk factors for early readmission after total pancreatectomy and islet auto transplantation* HPB, **20**, 166–174

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

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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. 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., Gołab, K., Cochet, O., Savari, O., Tibudan, M. et al (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 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 islet 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

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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

Damage, miRNA assessment

Saravanan, P.B., Kanak, M.A., Chang, C.A., Darden, C., Yoshimatsu G., Lawrence, M.C. and Naziruddin, B. (2018) *Islet damage during isolation as assessed by miRNAs and the correlation of miRNA levels with post-transplantation outcome in islet autotransplantation* Am. J. Transplant., **18**, 982-989

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

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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

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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. et al (2005) *Single-donor, marginal-dose islet transplantation in patients with type 1 diabetes J. Am. Med. Assoc.* 830-835

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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

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OptiPrep – Ficoll comparison

Mita, A., Ricordi, C., Messinger, S., Miki, A., Misawa, R., Barker, S., Molano, R.D., Haertter, R. et al (2010) *Anti-pro-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

Allogenic blood transfusion

Yoshimatsu, G., Shahbazov, R., Saracino, G., Lawrence, M.C., Kim, P.T., Onaca, N., Beecher, E.E., Naziruddin, B. and Levy, M.F. (2017) *The impact of allogenic blood transfusion on the outcomes of total pancreatectomy with islet autotransplantation* Am. J. Surg., **214**, 849-855

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

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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

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

Ihm, S-H., Matsumoto, I., Zhang, H.J., Ansit, 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

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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. 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
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- 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

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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 /allogeneic transplantation* 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

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