

Institution	Enzyme Used	Enzyme Dose	n	Mean IEQ ± 1 SD/g Pancreas	Switch Time Min	Undigested (%)
2005 Geneva University Hospital <sup>1</sup>	Liberase HI	2142 WU & 105 DMC U/organ	9	2360 ± 1,350	17 ± 3.0	NR
	NB-1 Collagenase/NB Protease	2001 WU & 30 DMC U/organ	14	4020 ± 1240	22 ± 3.0	NR
2009 University of California San Francisco <sup>2</sup>	Liberase HI	2420 ± 85 WU & 71,500 caseinase U/organ	9	4888 ± 1683	16 ± 1.7	28.5*
	NB-1 Collagenase/NB Protease	1747 ± 212 WU & 244 ± 21 DMC U/organ	14	5862 ± 1843	16 ± 2.0	32*
2010 Uppsala University <sup>3</sup>	Liberase HI	≤ 100 g 1 bottle ≥ 100 g 1.3 bottles	101	4010 ± 2332	26.9 ± 5.0	15.6 ± 1.3
	NB-1 Collagenase/NB Protease	≤ 100 g 1 bottle NB-1 & 130 DMC U NB Protease/organ ≥ 100 g 1.3 bottles NB-1 & 150 DMC U NB Protease/organ	96	2979 ± 1460	26.4 ± 5.9	18.0 ± 1.0
2010 University of Alberta <sup>4</sup>	Liberase MTF	NR	17	4249 ± 1748	17.5 ± 5.4	NR
	NB-1 Collagenase/NB Protease	NR	24	3836 ± 1911	17.0 ± 4.9	NR
2010 University of Minnesota <sup>5</sup>	Collagenase HA/Thermolysin	1 bottle HA & 12 mg Thermolysin/organ	14	4147 ± 1759	20.1 ± 4.1	18.9
	NB-1 Collagenase/NB Protease	1600-4696 WU & 100-404 DMC U/organ	27	2134 ± 1524	23.7 ± 5.5	21.5
2012 University of Minnesota <sup>6</sup>	New Enzyme Mixture: Collagenase HA & NB Protease	18-20 WU Collagenase HA & 1.25-1.5 DMC U/g tissue	12	5329 ± 2519	16.3 ± 5.5	18.6
	Liberase MTF	2200-2615 WU & 78,600-165,960 NP U/organ	4	2217 ± 1405	20.7 ± 2.1	19.6
	Collagenase HA/Thermolysin	2018-2200 WU & 3.15-3.42 million NP U/organ	37	3467 ± 1698	21.2 ± 4.2	18.8
	NB-1 Collagenase/NB Protease	1600-4400 WU & 96-300 DMC U/organ	24	2202 ± 1403	23.6 ± 5.5	20.9
2015 City of Hope <sup>7</sup>	Liberase HI	26.2 ± 10.9 WU & 781 ± 388 caseinase U/g tissue	61	3109 ± 1870	10.7 ± 2.8	36.4
	Liberase MTF	31.2 ± 8.6 WU & 1873 ± 762 caseinase U/g tissue	115	2773 ± 1781	11.6 ± 2.3	26.5
	Collagenase NB-1/NB Protease	27.2 ± 6.7 WU & 1.5 ± 0.6 DMC U/g tissue	40	2625 ± 1413	12.3 ± 3.2	38.3
2016 University of Minnesota <sup>8</sup>	Rec Collagenase/BP Protease	C2: 12 or 20 WU & C1: 100K or 200 K & BP Protease: 23,400 U/g body-tail pancreas	12	5209 ± 2267	18.7 ± 4.0	13.6 ± 4.0
	New Enzyme Mixture	18-20 WU Collagenase HA & 1.25-1.75 DMC U/g body-tail pancreas	12	4727 ± 2125	15.0 ± 2.0	16 ± 9.0
	Cizyme Collagenase HA + Cizyme Thermolysin	1 bottle HA & 12 mg Thermolysin/organ	18	3505 ± 2412	20.6 ± 4.4	19 ± 5.1
	Serva Collagenase NB-1 + NB Protease	1600-4400 WU & 96-300 DMC U/organ	12	2630 ± 1772	25 ± 5.0	23 ± 10
2018 City of Hope <sup>9</sup>	Collagenase Gold/BP Protease	9.9 ± 0.6 WU & 28,682 ± 2216 NP U/g tissue	8	3503 ± 2062	12.6 ± 2.0	32.1
	Liberase MTF	25 ± 0.5 WU & 1208 ± 46.5 NP U/g tissue	48	3551 ± 2162	12.3 ± 2.0	20.9
	NB-1 Collagenase/NB Protease	17.5 ± 1.2 WU & 2.2 ± 0.16 DMC U/g tissue	15	2918 ± 1069	12.9 ± 1.2	15.8
2018 University of Louisville <sup>10</sup>	Rec Collagenase/BP Protease	C1: 100,000 CDA U & C2: 12 WU & 23,400 NP U/g tissue	7	5535 ± 830	20 ± 2.1	16.7
	Rec Collagenase/BP Protease	C1: NR CDA U & C2: 20 WU & 23,400 NP U/g tissue	5	5455 ± 918	19 ± 2.9	15.7
	Collagenase HA/BP Protease	Collagenase 12 WU & 23,400 NP U/g tissue	5	2582 ± 925	22 ± 3.8	37.8
	Collagenase HA/BP Protease	Collagenase 20 WU & 23,400 NP U/g tissue	6	4946 ± 974	18 ± 5.1	20.1

CDA U = collagen degrading activity U DMC U = dimethyl casein U NP U = Neutral Protease U NR = Not reported WU = Wunsch Units \*see <https://icr.coh.org/docs/Abstracts/10032008/Szot.pdf>

Casinase U for Liberase HI and Liberase MTF are not equivalent. | Mass and activity of Roche MTF thermolysin and VitaCyte thermolysin are not equivalent.

<sup>1</sup> Bucher P, Mathe Z, Morel P, Bosco D, Andres A, Kurfuest M, et al. Assessment of a novel two-component enzyme preparation for human islet isolation and transplantation. *Transplantation*. 2005 Jan 15;79(1):91-7.

<sup>2</sup> Szot GL, Lee MR, Tavakol MM, Lang J, Dekovic F, Kerlan RK, et al. - Successful clinical islet isolation using a GMP-manufactured collagenase and neutral protease. - *Transplantation* 2009 27;88(6):753-6.

<sup>3</sup> Brandhorst H, Friberg A, Nilsson B, Andersson HH, Felldin M, Foss A, et al. Large-scale comparison of Liberase HI and collagenase NB1 utilized for human islet isolation. *Cell Transplant*. 2010;19(1):3-8.

<sup>4</sup> O'Gorman D, Kin T, Imes S, Pawlick R, Senior P, Shapiro AM. Comparison of Human Islet Isolation Outcomes Using a New Mammalian Tissue-Free Enzyme Versus Collagenase NB-1. *Transplantation*. 2010;90:255-59.

<sup>5</sup> Balamurugan AN, Breite AG, Anazawa T, Loganathan G, Wilhelm JJ, Papas KK, et al. Successful human islet isolation and transplantation indicating the importance of class 1 collagenase and collagen degradation activity assay. *Transplantation*. 2010;89(8):954-61.

<sup>6</sup> Balamurugan AN, Loganathan G, Bellin MD, Wilhelm JJ, Harmon J, Anazawa T, et al. A new enzyme mixture to increase the yield and transplant rate of autologous and allogeneic human islet products. *Transplantation*. 2012; 93(7):693-702.

<sup>7</sup> Qi M, Valiente L, McFadden B, Omori K, Bilbao S, Juan J, et al. The Choice of Enzyme for Human Pancreas Digestion is a Critical Factor for Increasing the Success of Islet Isolation. *Transplant Direct*. 2015;1(4). doi: 10.1097/TXD.0000000000000522.

<sup>8</sup> Balamurugan AN, Green ML, Breite AG, Loganathan G, Wilhelm JJ, Tweed B, et al. Identifying Effective Enzyme Activity Targets for Recombinant Class I and Class II Collagenase for Successful Human Islet Isolation. *Transplant Direct*. 2016;2(1):e54. doi: 10.1097/TXD.0000000000000563.

<sup>9</sup> Khatah B, Tucker A, Chen KT, Perez R, Bilbao S, Valiente L, et al. Evaluation of collagenase gold plus BP protease in isolating islets from human pancreata. *Islets*. 2018;10(2):51-9. doi: 10.1080/19382014.2017.1417716.

<sup>10</sup> Loganathan G, Subhashree V, Breite AG, Tucker WW, Narayanan S, Dhanasekaran M, et al. Beneficial effect of recombinant rC1rC2 collagenases on human islet function: Efficacy of low-dose enzymes on pancreas digestion and yield. *Am J Transplant*. 2018;18(2):478-85.