

## Documents

Sadikan, M.Z.<sup>a</sup>, Abdul Nasir, N.A.<sup>b</sup>, Lambuk, L.<sup>c</sup>, Mohamud, R.<sup>c</sup>, Reshidan, N.H.<sup>d</sup>, Low, E.<sup>e</sup>, Singar, S.A.<sup>f</sup>, Mohamad Sabere, A.S.<sup>g</sup>, Iezhitsa, I.<sup>h</sup>, Agarwal, R.<sup>h</sup>

**Diabetic retinopathy: a comprehensive update on in vivo, in vitro and ex vivo experimental models**  
(2023) *BMC Ophthalmology*, 23 (1), art. no. 421, .

DOI: 10.1186/s12886-023-03155-1

<sup>a</sup> Department of Pharmacology, Faculty of Medicine, Manipal University College Malaysia (MUCM), Bukit Baru, Melaka, 75150, Malaysia

<sup>b</sup> Centre for Neuroscience Research (NeuRon), Faculty of Medicine, Universiti Teknologi MARA, Selangor, Sungai Buloh, 47000, Malaysia

<sup>c</sup> Department of Immunology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, 16150, Malaysia

<sup>d</sup> School of Biology, Faculty of Applied Sciences, Universiti Teknologi MARA, Selangor, Shah Alam, 40450, Malaysia

<sup>e</sup> Ageing Biology Centre, Newcastle University, Newcastle upon Tyne, NE1 7RU, United Kingdom

<sup>f</sup> Department of Nutrition and Integrative Physiology, College of Health and Human Sciences, Florida State University, Tallahassee, FL 32306, United States

<sup>g</sup> Kulliyah of Pharmacy, International Islamic University Malaysia, Jalan Sultan Ahmad Shah, Bandar Indera Mahkota, Kuantan, Pahang, 25200, Malaysia

<sup>h</sup> School of Medicine, International Medical University, Bukit Jalil, Kuala Lumpur, 57000, Malaysia

<sup>i</sup> Department of Pharmacology and Bioinformatics, Volgograd State Medical University, Pavshikh Bortsov sq. 1, Volgograd, 400131, Russian Federation

### Abstract

Diabetic retinopathy (DR), one of the leading causes of visual impairment and blindness worldwide, is one of the major microvascular complications in diabetes mellitus (DM). Globally, DR prevalence among DM patients is 25%, and 6% have vision-threatening problems among them. With the higher incidence of DM globally, more DR cases are expected to be seen in the future. In order to comprehend the pathophysiological mechanism of DR in humans and discover potential novel substances for the treatment of DR, investigations are typically conducted using various experimental models. Among the experimental models, in vivo models have contributed significantly to understanding DR pathogenesis. There are several types of in vivo models for DR research, which include chemical-induced, surgical-induced, diet-induced, and genetic models. Similarly, for the in vitro models, there are several cell types that are utilised in DR research, such as retinal endothelial cells, Müller cells, and glial cells. With the advancement of DR research, it is essential to have a comprehensive update on the various experimental models utilised to mimic DR environment. This review provides the update on the in vitro, in vivo, and ex vivo models used in DR research, focusing on their features, advantages, and limitations. © 2023, BioMed Central Ltd., part of Springer Nature.

### Author Keywords

Diabetic retinopathy; Ex vivo; Experimental models; In vitro; In vivo

### Index Keywords

blindness, diabetes mellitus, diabetic retinopathy, endothelium cell, human, low vision, pathology, prevalence, retina; Blindness, Diabetes Mellitus, Diabetic Retinopathy, Endothelial Cells, Humans, Prevalence, Retina, Vision, Low

### References

- Saeedi, P., Petersohn, I., Salpea, P., Malanda, B., Karuranga, S., Unwin, N., Colagiuri, S., Ogurtsova, K.  
**Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas**  
(2019) *Diabetes Res Clin Pract*, 157, p. 107843.  
PID: 31518657
- Teo, Z.L., Tham, Y.-C., Yu, M.C.Y., Chee, M.L., Rim, T.H., Cheung, N., Bikbov, M.M., Lu, Y.  
**Global prevalence of Diabetic Retinopathy and Projection of Burden through 2045: systematic review and Meta-analysis**  
(2021) *Ophthalmology*, 128 (11), pp. 1580-1591.  
PID: 33940045

- Rakieten, N., Rakieten, M.L., Nadkarni, V.  
**Studies on the diabetogenic action of streptozotocin (NSC-37917)**  
(1963) *Cancer Chemother Rep*, 29, pp. 91-98.  
PID: 13990586
- Olivares, A.M., Althoff, K., Chen, G.F., Wu, S., Morrisson, M.A., DeAngelis, M.M., Haider, N.  
**Animal models of diabetic retinopathy**  
(2017) *Curr Diab Rep*, 17 (10), pp. 1-17.
- Furman, B.L.  
**Streptozotocin-induced diabetic models in mice and rats**  
(2015) *Curr Protoc Pharmacol*, 70 (1), pp. 5420-5471.
- Agarwal, M.  
**Streptozotocin: mechanisms of action**  
(1980) *FEBS Lett*, 120 (1), pp. 1-3.  
COI: 1:STN:280:DyaL3M%2FmslWisg%3D%3D, PID: 6108240
- Junod, A., Lambert, A., Orci, L., Pictet, R., Gonet, A., Renold, A.  
**Studies of the diabetogenic action of streptozotocin**  
(1967) *Proc Soc Exp Biol Med*, 126 (1), pp. 201-205.  
COI: 1:CAS:528:DyaF1cXhtFGrtw%3D%3D, PID: 4864021
- Gajdosik, A., Gajdosikova, A., Stefek, M., Navarova, J., Hozova, R.  
**Streptozotocin-induced experimental diabetes in male Wistar rats**  
(1999) *Gen Physiol Biophys*, 18, pp. 54-62.  
COI: 1:CAS:528:DC%2BD3cXhsVGqur0%3D, PID: 10703720
- Ghasemi, A., Khalifi, S., Jedi, S.  
**Streptozotocin-nicotinamide-induced rat model of type 2 diabetes**  
(2014) *Acta Physiol Hung*, 101 (4), pp. 408-420.
- Feit-Leichman, R.A., Kinouchi, R., Takeda, M., Fan, Z., Mohr, S., Kern, T.S., Chen, D.F.  
**Vascular damage in a mouse model of diabetic retinopathy: Relation to neuronal and glial changes**  
(2005) *Invest Ophthalmol Vis Sci*, 46 (11), pp. 4281-4287.
- Eleazu, C.O., Eleazu, K.C., Chukwuma, S., Essien, U.N.  
**Review of the mechanism of cell death resulting from streptozotocin challenge in experimental animals, its practical use and potential risk to humans**  
(2013) *J Diabetes Metab Disord*, 12 (1), pp. 1-7.
- Vieira, R., Souto, S.B., Sánchez-López, E., López Machado, A., Severino, P., Jose, S., Santini, A., García, M.L.  
**Sugar-lowering drugs for type 2 diabetes mellitus and metabolic syndrome—strategies for in vivo administration: Part-II**  
(2019) *J Clin Med*, 8 (9), p. 1332.
- Vique-Sánchez, J.L., López-Palacios, T.P., Miranda-Ozuna, J.F., Benítez-Cardoza, C.G.  
**Effects of W100E-Leptin in streptozotocin-induced diabetic mice**  
(2020) *Nutr Clin Y Diet Hosp*, 40 (3).
- Jin, D., Zhang, B., Li, Q., Tu, J., Zhou, B.  
**Effect of punicalagin on multiple targets in streptozotocin/high-fat diet-induced diabetic mice**  
(2020) *Food Funct*, 11 (12), pp. 10617-10634.
- Intine, R.V., Olsen, A.S., Sarras, M.P., Jr.  
**A zebrafish model of diabetes mellitus and metabolic memory**  
(2013) *J Vis Exp*, 72.

- Gardiner, T., Stitt, A., Anderson, H., Archer, D.  
**Selective loss of vascular smooth muscle cells in the retinal microcirculation of diabetic dogs**  
(1994) *Br J Ophthalmol*, 78 (1), pp. 54-60.  
COI: 1:STN:280:DyaK2c7ltlymsg%3D%3D, PID: 8110701
- McLetchie, N.  
**Alloxan diabetes: a discovery, albeit a minor one**  
(2002) *J R Coll Physicians Edinb*, 32 (2), pp. 134-142.  
COI: 1:STN:280:DC%2BD38nnsVSnsW%3D%3D, PID: 12434795
- Dixon, K.C., King, A., Malinin, T.  
**Protein in dying  $\beta$ -cells of the pancreatic islets**  
(1960) *Q J Exp Physiol Cogn Med Sci*, 45 (2), pp. 202-212.
- Rohilla, A., Ali, S.  
**Alloxan induced diabetes: Mechanisms and effects**  
(2012) *Int J Res Pharm Biomed Sci*, 3 (2), pp. 819-823.
- Borg, L.  
**Effects of alloxan on the islets of Langerhans: why does alloxan not stimulate insulin release?**  
(1981) *Ups J Med Sci*, 86 (2), pp. 189-195.  
COI: 1:CAS:528:DyaL3MXItV2nsb0%3D, PID: 7034349
- de Roethth, Pei, Y.F., Jr.  
**Experimental diabetic retinopathy: Retinal metabolism in the alloxan diabetic rat**  
(1960) *Arch Ophthalmol*, 63 (2), pp. 226-231.
- Engerman, R., Bloodworth, J.  
**Experimental diabetic retinopathy in dogs**  
(1965) *Arch Ophthalmol*, 73 (2), pp. 205-210.  
COI: 1:STN:280:DyaF2M%2Fkt1ajuW%3D%3D, PID: 14237790
- Kern, T.S., Engerman, R.L.  
**Comparison of retinal lesions in alloxan-diabetic rats and galactose-fed rats**  
(1994) *Curr Eye Res*, 13 (12), pp. 863-867.  
COI: 1:STN:280:DyaK2M3js1yisW%3D%3D, PID: 7720392
- Radenković, M., Stojanović, M., Prostran, M.  
**Experimental diabetes induced by alloxan and streptozotocin: The current state of the art**  
(2016) *J Pharmacol Toxicol Methods*, 78, pp. 13-31.
- Zarebska, A., Czerny, K., Bakiera, K., Cichacz-Kwiatkowska, B., Lis-Sochocka, M., Kiś, G., Wojtowicz, Z.  
**Histological changes in the retina in experimental alloxan-induced diabetes in rabbits**  
(2001) *Ann Univ Mariae Curie Sklodowska Med*, pp. 81-84.
- Szkudelski, T.  
**The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas**  
(2001) *Physiol Res*, 50 (6), pp. 537-546.
- Misra, M., Aiman, U.  
**Alloxan: an unpredictable drug for diabetes induction?**  
(2012) *Indian J Pharmacol*, 44 (4), pp. 538-539.  
COI: 1:CAS:528:DC%2BC38XhsVemsL7I, PID: 23087526

- Lenzen, S.  
**The mechanisms of alloxan-and streptozotocin-induced diabetes**  
(2008) *Diabetologia*, 51 (2), pp. 216-226.
- Weerasekera, L.Y., Balmer, L.A., Ram, R., Morahan, G.  
**Characterization of retinal vascular and neural damage in a novel model of diabetic retinopathy**  
(2015) *Invest Ophthalmol Vis Sci*, 56 (6), pp. 3721-3730.
- Kumar, S., Zhuo, L.  
**Longitudinal in vivo imaging of retinal gliosis in a diabetic mouse model**  
(2010) *Exp Eye Res*, 91 (4), pp. 530-536.  
COI: 1:CAS:528:DC%2BC3cXhtFGjt7vI, PID: 20655908
- Gaucher, D., Chiappore, J.-A., Pâques, M., Simonutti, M., Boitard, C., Sahel, J.A., Massin, P., Picaud, S.  
**Microglial changes occur without neural cell death in diabetic retinopathy**  
(2007) *Vis Res*, 47 (5), pp. 612-623.
- Schröder, S., Palinski, W., Schmid-Schönbein, G.  
**Activated monocytes and granulocytes, capillary nonperfusion, and neovascularization in diabetic retinopathy**  
(1991) *Am J Pathol*, 139 (1), pp. 81-100.
- Su, L., Ji, J., Bian, J., Fu, Y., Ge, Y., Yuan, Z.  
**Tacrolimus (FK506) prevents early retinal neovascularization in streptozotocin-induced diabetic mice**  
(2012) *Int Immunopharmacol*, 14 (4), pp. 606-612.  
COI: 1:CAS:528:DC%2BC38XhslOku7fM, PID: 23032068
- Kuiper, E.J., Zijderveld Rv, Roestenberg, P., Lyons, K.M., Goldschmeding, R., Klaassen, I., Noorden, C.J.V., Schlingemann, R.O.  
**Connective tissue growth factor is necessary for retinal capillary basal lamina thickening in diabetic mice**  
(2008) *J Histochem Cytochem*, 56 (8), pp. 785-792.  
COI: 1:CAS:528:DC%2BD1cXos1Cjurw%3D, PID: 18474939
- Gubitosi-Klug, R.A., Talahalli, R., Du, Y., Nadler, J.L., Kern, T.S.  
**5-Lipoxygenase, but not 12/15-lipoxygenase, contributes to degeneration of retinal capillaries in a mouse model of diabetic retinopathy**  
(2008) *Diabetes*, 57 (5), pp. 1387-1393.
- Zheng, L., Du, Y., Miller, C., Gubitosi-Klug, R., Kern, T., Ball, S., Berkowitz, B.  
**Critical role of inducible nitric oxide synthase in degeneration of retinal capillaries in mice with streptozotocin-induced diabetes**  
(2007) *Diabetologia*, 50 (9), pp. 1987-1996.
- Kubota, S., Ozawa, Y., Kurihara, T., Sasaki, M., Yuki, K., Miyake, S., Noda, K., Tsubota, K.  
**Roles of AMP-activated protein kinase in diabetes-induced retinal inflammation**  
(2011) *Invest Ophthalmol Vis Sci*, 52 (12), pp. 9142-9148.
- Li, G., Tang, J., Du, Y., Lee, C.A., Kern, T.S.  
**Beneficial effects of a novel RAGE inhibitor on early diabetic retinopathy and tactile allodynia**  
(2011) *Mol Vis*, 17, pp. 3156-3165.
- Wang, Z., Yadav, A.S., Leskova, W., Harris, N.R.  
**Attenuation of streptozotocin-induced microvascular changes in the mouse retina with the endothelin receptor A antagonist atrasentan**  
(2010) *Exp Eye Res*, 91 (5), pp. 670-675.  
COI: 1:CAS:528:DC%2BC3cXhtlCjsbzJ, PID: 20727883

- Wright, W.S., Harris, N.R.  
**Ozagrel attenuates early streptozotocin-induced constriction of arterioles in the mouse retina**  
(2008) *Exp Eye Res*, 86 (3), pp. 528-536.  
COI: 1:CAS:528:DC%2BD1cXivFyltb0%3D, PID: 18262522
- Kurihara, T., Ozawa, Y., Nagai, N., Shinoda, K., Noda, K., Imamura, Y., Tsubota, K., Ishida, S.  
**Angiotensin II type 1 receptor signaling contributes to synaptophysin degradation and neuronal dysfunction in the diabetic retina**  
(2008) *Diabetes*, 57 (8), pp. 2191-2198.
- Sasaki, M., Ozawa, Y., Kurihara, T., Kubota, S., Yuki, K., Noda, K., Kobayashi, S., Tsubota, K.  
**Neurodegenerative influence of oxidative stress in the retina of a murine model of diabetes**  
(2010) *Diabetologia*, 53 (5), pp. 971-979.  
COI: 1:CAS:528:DC%2BC3cXktlGgtbY%3D, PID: 20162412
- Martin, P.M., Roon, P., van Ells, T.K., Ganapathy, V., Smith, S.B.  
**Death of retinal neurons in streptozotocin-induced diabetic mice**  
(2004) *Invest Ophthalmol Vis Sci*, 45 (9), pp. 3330-3336.
- Yang, Y., Hayden, M.R., Sowers, S., Bagree, S.V., Sowers, J.R.  
**Retinal redox stress and remodeling in cardiometabolic syndrome and diabetes**  
(2010) *Oxid Med Cell Longev*, 3 (6), pp. 392-403.  
PID: 21307645
- Howell, S.J., Mekhail, M.N., Azem, R., Ward, N.L., Kern, T.S.  
**Degeneration of retinal ganglion cells in diabetic dogs and mice: relationship to glycemic control and retinal capillary degeneration**  
(2013) *Mol Vis*, 19, p. 1413.
- Aizu, Y., Oyanagi, K., Hu, J., Nakagawa, H.  
**Degeneration of retinal neuronal processes and pigment epithelium in the early stage of the streptozotocin-diabetic rats**  
(2002) *Neuropathol*, 22 (3), pp. 161-170.
- Zhang, J., Wu, Y., Jin, Y., Ji, F., Sinclair, S.H., Luo, Y., Xu, G., Yanoff, M.  
**Intravitreal injection of erythropoietin protects both retinal vascular and neuronal cells in early diabetes**  
(2008) *Invest Ophthalmol Vis Sci*, 49 (2), pp. 732-742.  
PID: 18235022
- Deguchi, S., Otake, H., Nakazawa, Y., Hiramatsu, N., Yamamoto, N., Nagai, N.  
**Ophthalmic formulation containing nilvadipine nanoparticles prevents retinal dysfunction in rats injected with streptozotocin**  
(2017) *Int J Mol Sci*, 18 (12), p. 2720.
- Qiu, F., Zhu, M., Le, Y.Z.  
**Noninvasive diagnosis of regional alteration of retinal morphology and structure with optical coherence tomography in rodents**  
(2019) *Adv Exp Med Biol*, 1185, pp. 151-155.  
COI: 1:CAS:528:DC%2BB3cXhsVegsb3L, PID: 31884604
- Lu, L.C., Zhou, W., Li, Z.H., Yu, C.P., Li, C.W., LuoH-h, Xie, H.  
**Effects of arctiin on streptozotocin-induced diabetic retinopathy in Sprague-Dawley rats**  
(2012) *Planta Med*, 78 (12), pp. 1317-1323.  
COI: 1:CAS:528:DC%2BC38XhsFGru7vN, PID: 22753037

- Yu, X., Xu, Z., Mi, M., Xu, H., Zhu, J., Wei, N., Chen, K., Wang, J.  
**Dietary taurine supplementation ameliorates diabetic retinopathy via anti-excitotoxicity of glutamate in streptozotocin-induced Sprague-Dawley rats**  
(2008) *Neurochem Res*, 33, pp. 500-507.  
COI: 1:CAS:528:DC%2BD1cXhs1ahsb8%3D, PID: 17762918
- Kern, T., Miller, C., Tang, J., Du, Y., Ball, S., Berti-Matera, L.  
**Comparison of three strains of diabetic rats with respect to the rate at which retinopathy and tactile allodynia develop**  
(2010) *Mol Vis*, 16, p. 1629.  
COI: 1:CAS:528:DC%2BC3cXhtVGqt7vE, PID: 20806092
- Rungger-Brändle, E., Dosso, A.A., Leuenberger, P.M.  
**Glial reactivity, an early feature of diabetic retinopathy**  
(2000) *Invest Ophthalmol Vis Sci*, 41 (7), pp. 1971-1980.  
PID: 10845624
- Li, L., Li, Y.L., Zhou, Y.F., Ge, Z.Y., Wang, L.L., Li, Z.Q., Guo, Y.J., Liu, J.X.  
**Jiangtang Xiaozhi recipe prevents diabetic retinopathy in streptozotocin-induced diabetic rats**  
(2017) *Chin J Integr Med*, 23 (6), pp. 425-432.  
PID: 27338824
- Anderson, H., Stitt, A., Gardiner, T., Lloyd, S., Archer, D.  
**Induction of alloxan/streptozotocin diabetes in dogs: a revised experimental technique**  
(1993) *Lab Anim*, 27 (3), pp. 281-285.  
COI: 1:STN:280:DyaK3sznsFKrtA%3D%3D, PID: 8366676
- Li, Q., Zemel, E., Miller, B., Perlman, I.  
**Early retinal damage in experimental diabetes: electroretinographical and morphological observations**  
(2002) *Exp Eye Res*, 74 (5), pp. 615-625.  
COI: 1:CAS:528:DC%2BD38Xlt1ylt74%3D, PID: 12076083
- Ly, A., Yee, P., Vessey, K.A., Phipps, J.A., Jobling, A.I., Fletcher, E.L.  
**Early inner retinal astrocyte dysfunction during diabetes and development of hypoxia, retinal stress, and neuronal functional loss**  
(2011) *Invest Ophthalmol Vis Sci*, 52 (13), pp. 9316-9326.  
COI: 1:CAS:528:DC%2BC38XjtVKrsrY%3D, PID: 22110070
- Zeng, X.X., NG, Y., Ling, E.A.  
**Neuronal and microglial response in the retina of streptozotocin-induced diabetic rats**  
(2000) *Vis Neurosci*, 17 (3), pp. 463-471.  
COI: 1:STN:280:DC%2BD3M%2FjsVGktw%3D%3D, PID: 10910112
- Si, Y.F., Wang, J., Guan, J., Zhou, L., Sheng, Y., Zhao, J.  
**Treatment with hydrogen sulfide alleviates streptozotocin-induced diabetic retinopathy in rats**  
(2013) *Br J Pharmacol*, 169 (3), pp. 619-631.  
COI: 1:CAS:528:DC%2BC3sXptlOhsbY%3D, PID: 23488985
- Jariyapongskul, A., Rungjaroen, T., Kasetsuwan, N., Patumraj, S., Seki, J., Niimi, H.  
**Long-term effects of oral vitamin C supplementation on the endothelial dysfunction in the iris microvessels of diabetic rats**  
(2007) *Microvasc Res*, 74 (1), pp. 32-38.  
COI: 1:CAS:528:DC%2BD2sXmtlWgu7c%3D, PID: 17467747

- Anderson, H., Stitt, A., Gardiner, T., Archer, D.  
**Diabetic retinopathy: morphometric analysis of basement membrane thickening of capillaries in different retinal layers within arterial and venous environments**  
(1995) *Br J Ophthalmol*, 79 (12), pp. 1120-1123.  
COI: 1:STN:280:DyaK287msVyqtQ%3D%3D, PID: 8562548
- Sadikan, M.Z., Abdul Nasir, N.A., Iezhitsa, I., Agarwal, R.  
**Open field mirror test as a tool for the assessment of visual functions in rats with streptozotocin-induced diabetes**  
(2021) *Neurosci Res Notes*, 4 (3), pp. 11-20.
- Hancock, H.A., Kraft, T.W.  
**Oscillatory potential analysis and ERGs of normal and diabetic rats**  
(2004) *Invest Ophthalmol Vis Sci*, 45 (3), pp. 1002-1008.  
PID: 14985323
- Sadikan, M.Z., Abdul Nasir, N.A., Iezhitsa, I., Agarwal, R.  
**Antioxidant and anti-apoptotic effects of tocotrienol-rich fraction against streptozotocin-induced diabetic retinopathy in rats**  
(2022) *Biomed Pharmacother*, 153.
- Sadikan, M.Z., Abdul Nasir, N.A., Bakar, N.S., Iezhitsa, I., Agarwal, R.  
**Tocotrienol-rich fraction reduces retinal inflammation and angiogenesis in rats with streptozotocin-induced diabetes**  
(2023) *BMC Complement Med Ther*, 23 (1).  
(.),.,, <https://doi.org/10.1186/s12906-023-04005-9>
- Drago, F., La Manna, C., Emmi, I., Marino, A.  
**Effects of sulfinpyrazone on retinal damage induced by experimental diabetes mellitus in rabbits**  
(1998) *Pharmacol Res*, 38 (2), pp. 97-100.  
COI: 1:CAS:528:DyaK1cXIsFeitbo%3D, PID: 9721595
- Kador, P.F., Takahashi, Y., Akagi, Y., Blessing, K., Randazzo, J., Wyman, M.  
**Age-dependent retinal capillary pericyte degeneration in galactose-fed dogs**  
(2007) *J Ocul Pharmacol Ther*, 23 (1), pp. 63-69.  
COI: 1:CAS:528:DC%2BD2sXisVGis7c%3D, PID: 17341153
- Lee, S.E., Ma, W., Rattigan, E.M., Aleshin, A., Chen, L., Johnson, L.L., D'Agati, V.D., Barile, G.R.  
**Ultrastructural features of retinal capillary basement membrane thickening in diabetic swine**  
(2010) *Ultrastruct Pathol*, 34 (1), pp. 35-41.  
PID: 20070152
- Hainsworth, D.P., Katz, M.L., Sanders, D.A., Sanders, D.N., Wright, E.J., Sturek, M.  
**Retinal capillary basement membrane thickening in a porcine model of diabetes mellitus**  
(2002) *Comp Med*, 52 (6), pp. 523-529.  
COI: 1:CAS:528:DC%2BD3sXktlGisA%3D%3D, PID: 12540165
- Tso, M., Kurosawa, A., Benhamou, E., Bauman, A., Jeffrey, J., Jonasson, O.  
**Microangiopathic retinopathy in experimental diabetic monkeys**  
(1988) *Trans Am Ophthalmol Soc*, 86, pp. 389-421.  
COI: 1:STN:280:DyaL1M3mvVSqtw%3D%3D, PID: 2980946
- Spadella, C.T., Machado, J.L.M., Lerco, M.M., Ortolan, E., Schellini, S.A., Gregório, E.  
**Temporal relationship between successful pancreas transplantation and control of ocular complications in alloxan-induced diabetic rats**  
(2008) *Transplant Proc*, pp. 518-523.  
Elsevier

- Doczi-Keresztesi, Z., Jung, J., Kiss, I., Mezei, T., Szabo, L., Ember, I.  
**Retinal and renal vascular permeability changes caused by stem cell stimulation in alloxan-induced diabetic rats, measured by extravasation of fluorescein**  
(2012) *In Vivo*, 26 (3), pp. 427-435.  
COI: 1:STN:280:DC%2BC38rntVSqug%3D%3D, PID: 22523295
- King, J.L., Mason, J.O., Cartner, S.C., Guidry, C.  
**The influence of alloxan-induced diabetes on Müller cell contraction-promoting activities in vitreous**  
(2011) *Invest Ophthalmol Vis Sci*, 52 (10), pp. 7485-7491.  
COI: 1:CAS:528:DC%2BC3MXhtlWku7vF, PID: 21862656
- Rastellini, C., Shapiro, R., Corry, R., Fung, J., Starzl, T., Rao, A.  
**An attempt to reverse diabetes by delayed islet cell transplantation in humans**  
(1997) *Transplant Proc: 1997: NIH Public Access*, 2238.
- Banting, F., Best, C.  
**Pancreatic extracts**  
(1922) *J Lab Clin Med*, 115 (2), pp. 254-272.
- Pfeiffer, E.F.  
(1969) *Handbook of Diabetes Mellitus*, 1.  
JF Lehmanns Verlag
- Maqbool, M., Dar, M.A., Gani, I., Mir, S.A.  
**Animal models in diabetes mellitus: an overview**  
(2019) *J Drug Deliv Ther*, 9 (1-s), pp. 472-475.  
COI: 1:CAS:528:DC%2BC1MXht1Crt7rN
- Kumar, S., Singh, R., Vasudeva, N., Sharma, S.  
**Acute and chronic animal models for the evaluation of anti-diabetic agents**  
(2012) *Cardiovasc Diabetol*, 11 (1), pp. 1-13.
- Mansour, S., Hatchell, D., Chandler, D., Saloupis, P., Hatchell, M.  
**Reduction of basement membrane thickening in diabetic cat retina by sulindac**  
(1990) *Invest Ophthalmol Vis Sci*, 31 (3), pp. 457-463.
- Hatchell, D.L.  
**Diabetic retinopathy in a cat**  
(1995) *Exp Eye Res*, 60, pp. 591-593.  
COI: 1:STN:280:DyaK2MzjvF2itA%3D%3D, PID: 7615025
- Linsenmeier, R.A., Braun, R.D., McRipley, M.A., Padnick, L.B., Ahmed, J., Hatchell, D., McLeod, D.S., Lutty, G.A.  
**Retinal hypoxia in long-term diabetic cats**  
(1998) *Invest Ophthalmol Vis Sci*, 39, pp. 1647-1657.  
COI: 1:STN:280:DyaK1czmtlWgtg%3D%3D, PID: 9699554
- Kim, S.Y., Johnson, M.A., McLeod, D.S., Alexander, T., Otsuji, T., Steidl, S.M., Hansen, B.C., Lutty, G.A.  
**Retinopathy in monkeys with spontaneous type 2 diabetes**  
(2004) *Invest Ophthalmol Vis Sci*, 45 (12), pp. 4543-4553.  
PID: 15557466
- Beigrezaei, S., Ghiasvand, R., Feizi, A., Iraj, B.  
**Relationship between dietary patterns and incidence of type 2 diabetes**  
(2019) *Int J Prev Med*, 10, p. 122.
- Sami, W., Ansari, T., Butt, N.S., Ab Hamid, M.R.  
**Effect of diet on type 2 diabetes mellitus: a review**



(2017) *Int J Health Sci (Qassim)*, 11 (2), pp. 65-71.

PID: 28539866

- Engerman, R.L., Kern, T.S.  
**Experimental galactosemia produces diabetic-like retinopathy**  
(1984) *Diabetes*, 33 (1), pp. 97-100.  
COI: 1:CAS:528:DyaL2cXms1WitQ%3D%3D, PID: 6360771
- Chang, R.C., Shi, L., Huang, C.C., Kim, A.J., Ko, M.L., Zhou, B., Ko, G.Y.  
**High-fat diet-induced retinal dysfunction**  
(2015) *Invest Ophthalmol Vis Sci*, 56 (4), pp. 2367-2380.  
COI: 1:CAS:528:DC%2BC28XnvVOisLg%3D, PID: 25788653
- Asare-Bediako, B., Noothi, S.K., Li Calzi, S., Athmanathan, B., Vieira, C.P., Adu-Agyeiwaah, Y., Dupont, M., Levi, M.  
**Characterizing the retinal phenotype in the high-fat diet and western diet mouse models of prediabetes**  
(2020) *Cells*, 9 (2), p. 464.
- Clarkson-Townsend, D.A., Douglass, A.J., Singh, A., Allen, R.S., Uwaifo, I.N., Pardue, M.T.  
**Impacts of high fat diet on ocular outcomes in rodent models of visual disease**  
(2021) *Exp Eye Res*, 204.  
<https://doi.org/10.1016/j.exer.2021.108440>
- Kowluru, R.A.  
**Retinopathy in a diet-induced type 2 diabetic rat model and role of epigenetic modifications**  
(2020) *Diabetes*, 69 (4), pp. 689-698.
- Barrière, D.A., Noll, C., Roussy, G., Lizotte, F., Kessai, A., Kirby, K., Belleville, K., Geraldès, P.  
**Combination of high-fat/high-fructose diet and low-dose streptozotocin to model long-term type-2 diabetes complications**  
(2018) *Sci Rep*, 8 (1), p. 424.
- Zhang, Q., Xiao, X., Zheng, J., Li, M., Yu, M., Ping, F., Wang, T., Wang, X.  
**Compound danshen dripping pill inhibits retina cell apoptosis in diabetic rats**  
(2018) *Front Physiol*, 9, p. 1501.
- Skovsø, S.  
**Modeling type 2 diabetes in rats using high fat diet and streptozotocin**  
(2014) *J Diabetes Investig*, 5 (4), pp. 349-358.  
PID: 25411593
- Jo, D.H., Cho, C.S., Kim, J.H., Jun, H.O., Kim, J.H.  
**Animal models of diabetic retinopathy: doors to investigate pathogenesis and potential therapeutics**  
(2013) *J Biomed Sci*, 20 (1), pp. 1-13.
- Kador, P.F., Akagi, Y., Takahashi, Y., Ikebe, H., Wyman, M., Kinoshita, J.H.  
**Prevention of retinal vessel changes associated with diabetic retinopathy in galactose-fed dogs by aldose reductase inhibitors**  
(1990) *Arch Ophthalmol*, 108 (9), pp. 1301-1309.  
COI: 1:STN:280:DyaK3cznvFyrsA%3D%3D, PID: 2119169
- Robinson, W.G., Jr., Laver, N.M., Lou, M.F.  
**The role of aldose reductase in diabetic retinopathy: prevention and intervention studies**  
(1995) *Prog Retin Eye Res*, 14 (2), pp. 593-640.

- Kern, T.S., Engerman, R.L.  
**Comparison of retinal lesions in alloxan-diabetic rats and galactose-fed rats**  
(1994) *Curr Eye Res*, 1 (12), pp. 863-867.
- Roy, S., Lorenzi, M.  
**Early biosynthetic changes in the diabetic-like retinopathy of galactose-fed rats**  
(1996) *Diabetologia*, 39, pp. 735-738.  
COI: 1:CAS:528:DyaK28XktF2msrc%3D, PID: 8781771
- Kobayashi, T., Kubo, E., Takahashi, Y., Kasahara, T., Yonezawa, H., Akagi, Y.  
**Retinal vessel changes in galactose-fed dogs**  
(1998) *Arch Ophthalmol*, 116 (6), pp. 785-789.  
COI: 1:CAS:528:DyaK1cXktFyju7Y%3D, PID: 9639449
- Joussem, A.M., Doehmen, S., Le, M.L., Koizumi, K., Radetzky, S., Krohne, T.U., Poulaki, V., Kociok, N.  
**TNF- $\alpha$  mediated apoptosis plays an important role in the development of early diabetic retinopathy and long-term histopathological alterations**  
(2009) *Mol Vis*, 15, pp. 1418-1428.  
COI: 1:CAS:528:DC%2BD1MXhtVShtr%2FO, PID: 19641635
- Kern, T.S., Engerman, R.L.  
**A mouse model of diabetic retinopathy**  
(1996) *Arch Ophthalmol*, 114 (8), pp. 986-990.  
COI: 1:STN:280:DyaK28zis1Wqug%3D%3D, PID: 8694735
- Joussem, A.M., Poulaki, V., Le, M.L., Koizumi, K., Esser, C., Janicki, H., Schraermeyer, U., Kirchhof, B.  
**A central role for inflammation in the pathogenesis of diabetic retinopathy**  
(2004) *FASEB J*, 18 (12), pp. 1450-1452.  
COI: 1:CAS:528:DC%2BD2cXntIKktLs%3D, PID: 15231732
- Azrad-Leibovich, T., Zahavi, A., Gohas, M.F., Brookman, M., Barinfeld, O., Muhsinoglu, O., Michowiz, S., Goldenberg-Cohen, N.  
**Characterization of Diabetic Retinopathy in two mouse models and response to a single injection of anti-vascular endothelial growth factor**  
(2022) *Int J Mol Sci*, 24 (1), p. 324.
- Jiang, X., Yang, L., Luo, Y.  
**Animal models of diabetic retinopathy**  
(2015) *Curr Eye Res*, 40 (8), pp. 761-771.  
COI: 1:CAS:528:DC%2BC2MXhtFyqs7vP, PID: 25835487
- Barber, A.J., Antonetti, D.A., Kern, T.S., Reiter, C.E., Soans, R.S., Krady, J.K., Levison, S.W., Bronson, S.K.  
**The Ins2Akita mouse as a model of early retinal complications in diabetes**  
(2005) *Invest Ophthalmol Vis Sci*, 46 (6), pp. 2210-2218.  
PID: 15914643
- Bogdanov, P., Corraliza, L., Villena, A., Carvalho, J., Garcia-Arumi, A.R., Ramos, J., Ruberte, D., Hernandez, R.  
**The db/db mouse: a useful model for the study of diabetic retinal neurodegeneration**  
(2014) *PLoS ONE*, 9 (5).  
PID: 24837086
- Rakoczy, E.P., Rahman, I.S.A., Binz, N., Li, C.-R., Vagaja, N.N., de Pinho, M., Lai, C.-M.  
**Characterization of a mouse model of hyperglycemia and retinal neovascularization**  
(2010) *Am J Pathol*, 177 (5), pp. 2659-2670.  
PID: 20829433

- Chaurasia, S.S., Lim, R.R., Parikh, B.H., Wey, Y.S., Tun, B.B., Wong, T.Y., Luu, C.D., Rackoczy, E.  
**The NLRP3 inflammasome may contribute to pathologic neovascularization in the advanced stages of diabetic retinopathy**  
(2018) *Sci Rep*, 8 (1), p. 2847.  
PID: 29434227
- Schmidt, R.E., Dorsey, D.A., Beaudet, L.N., Peterson, R.G.  
**Analysis of the Zucker Diabetic fatty (ZDF) type 2 diabetic rat model suggests a neurotrophic role for insulin/IGF-I in diabetic autonomic neuropathy**  
(2003) *Am J Pathol*, 163 (1), pp. 21-28.  
COI: 1:CAS:528:DC%2BD3sXmtVWrt7o%3D, PID: 12819007
- Schroeder, M., Zagoory-Sharon, O., Shbiro, L., Marco, A., Hyun, J., Moran, T.H., Bi, S., Weller, A.  
**Development of obesity in the Otsuka Long-Evans Tokushima fatty rat**  
(2009) *Am J Physiol Regul Integr Comp Physiol*, 297 (6), pp. R1749-R1760.  
COI: 1:CAS:528:DC%2BD1MXhsFOltb7K, PID: 19793959
- Akimoto, T., Nakama, K., Katsuta, Y., Zhang, X.-J., Ohsuga, M., Ishizaki, M., Sawai, N., Ozawa, H.  
**Characterization of a novel congenic strain of diabetic fatty (WBN/Kob-Leprfa) rat**  
(2008) *Biochem Biophys Res Commun*, 366 (2), pp. 556-562.  
COI: 1:CAS:528:DC%2BD1cXhsV2qsw%3D%3D, PID: 18068663
- Masuyama, T., Komeda, K., Hara, A., Noda, M., Shinohara, M., Oikawa, T., Kanazawa, Y., Taniguchi, K.  
**Chronological characterization of diabetes development in male spontaneously Diabetic Torii rats**  
(2004) *Biochem Biophys Res Commun*, 314 (3), pp. 870-877.  
COI: 1:CAS:528:DC%2BD2cXltF2htA%3D%3D, PID: 14741717
- Guest, P.C.  
**Characterization of the Goto-Kakizaki (GK) rat model of type 2 diabetes**  
(2019) *Methods Mol Biol*, 1916, pp. 203-211.
- Izumi, T., Yokota-Hashimoto, H., Zhao, S., Wang, J., Halban, P.A., Takeuchi, T.  
**Dominant negative pathogenesis by mutant proinsulin in the Akita diabetic mouse**  
(2003) *Diabetes*, 52 (2), pp. 409-416.  
COI: 1:CAS:528:DC%2BD3sXhtFans7g%3D, PID: 12540615
- Wang, J., Takeuchi, T., Tanaka, S., Kubo, S.-K., Kayo, T., Lu, D., Takata, K., Izumi, T.  
**A mutation in the insulin 2 gene induces diabetes with severe pancreatic  $\beta$ -cell dysfunction in the Mody mouse**  
(1999) *J Clin Investig*, 103 (1), pp. 27-37.  
COI: 1:CAS:528:DyaK1MXjsl2msw%3D%3D, PID: 9884331
- Leiter, E.H.  
**The NOD mouse: a model for analyzing the interplay between heredity and environment in development of autoimmune disease**  
(1993) *ILAR J*, 35 (1), pp. 4-14.
- Serreze, D.V., Chapman, H.D., Varnum, D.S., Gerling, I., Leiter, E.H., Shultz, L.D.  
**Initiation of autoimmune diabetes in NOD/Lt mice is MHC class I-dependent**  
(1997) *J Immunol*, 158 (8), pp. 3978-3986.  
COI: 1:CAS:528:DyaK2sXisFCqsbY%3D, PID: 9103469
- Pearson, J.A., Wong, F.S., Wen, L.  
**The importance of the non obese Diabetic (NOD) mouse model in autoimmune diabetes**

- (2016) *J Autoimmun*, 66, pp. 76-88.  
COI: 1:CAS:528:DC%2BC2MXhsFehsbbK, PID: 26403950
- Thayer, T.C., Wilson, S.B., Mathews, C.E.  
**Use of nonobese diabetic mice to understand human type 1 diabetes**  
(2010) *Endocrin Metab Clin*, 39 (3), pp. 541-561.  
COI: 1:CAS:528:DC%2BC3cXhtVGqsr3M
  - Chen, H., Charlat, O., Tartaglia, L.A., Woolf, E.A., Weng, X., Ellis, S.J., Lakey, N.D., Breitbart, R.E.  
**Evidence that the diabetes gene encodes the leptin receptor: identification of a mutation in the leptin receptor gene in db/db mice**  
(1996) *Cell*, 84 (3), pp. 491-495.  
COI: 1:CAS:528:DyaK28XhtFWqt7s%3D, PID: 8608603
  - Hummel, K.P., Dickie, M.M., Coleman, D.L.  
**Diabetes, a new mutation in the mouse**  
(1966) *Science*, 153 (3740), pp. 1127-1128.  
COI: 1:STN:280:DyaF2s%2Fhs1WrtA%3D%3D, PID: 5918576
  - Okamoto, N., Tobe, T., Hackett, S.F., Ozaki, H., Vinos, M.A., LaRochelle, W., Zack, D.J., Campochiaro, P.A.  
**Transgenic mice with increased expression of vascular endothelial growth factor in the retina: a new model of intraretinal and subretinal neovascularization**  
(1997) *Am J Pathol*, 151 (1), pp. 281-291.  
COI: 1:CAS:528:DyaK2sXkslartb8%3D, PID: 9212753
  - Tee, L., Penrose, M., O'Shea, J., Lai, C.-M., Rakoczy, E., Dunlop, S.  
**VEGF-induced choroidal damage in a murine model of retinal neovascularisation**  
(2008) *Br J Ophthalmol*, 92 (6), pp. 832-838.  
COI: 1:STN:280:DC%2BD1czlvV2ltw%3D%3D, PID: 18523088
  - McLenachan, S., Magno, A.L., Ramos, D., Catita, J., McMenamin, P.G., Chen, F.K., Rakoczy, E.P., Ruberte, J.  
**Angiography reveals novel features of the retinal vasculature in healthy and diabetic mice**  
(2015) *Exp Eye Res*, 138, pp. 6-21.  
COI: 1:CAS:528:DC%2BC2MXhtVynsLfP, PID: 26122048
  - Yokoi, N., Hoshino, M., Hidaka, S., Yoshida, E., Beppu, M., Hoshikawa, R., Sudo, K., Seino, S.  
**A novel rat model of type 2 diabetes: the Zucker fatty diabetes mellitus ZFDM rat**  
(2013) *J Diabetes Res*, 2013, p. 103731.
  - Miyamoto, K., Hiroshiba, N., Tsujikawa, A., Ogura, Y.  
**In vivo demonstration of increased leukocyte entrapment in retinal microcirculation of diabetic rats**  
(1998) *Invest Ophthalmol Vis Sci*, 39 (11), pp. 2190-2194.
  - Watanabe, T.K., Suzuki, M., Yamasaki, Y., Okuno, S., Hishigaki, H., Ono, T., Oga, K., Kanemoto, N.  
**Mutated G-protein-coupled receptor GPR10 is responsible for the hyperphagia/dyslipidaemia/obesity locus of Dmo1 in the OLETF rat**  
(2005) *Clin Exp Pharmacol Physiol*, 32 (5-6), pp. 355-366.  
COI: 1:CAS:528:DC%2BD2MXksFGtrtg%3D, PID: 15854142
  - Lu, Z.Y., Bhutto, I.A., Amemiya, T.  
**Retinal changes in Otsuka long-evans Tokushima fatty rats (spontaneously diabetic rat)—possibility of a new experimental model for diabetic retinopathy**  
(2003) *Jpn J Ophthalmol*, 47 (1), pp. 28-35.  
PID: 12586175

- Hornum, L., Rømer, J., Markholst, H.  
**The diabetes-prone BB rat carries a frameshift mutation in *Ian4*, a positional candidate of *Iddm1***  
(2002) *Diabetes*, 51 (6), pp. 1972-1979.
- MacMurray, A.J., Moralejo, D.H., Kwitek, A.E., Rutledge, E.A., Van Yserloo, B., Gohlke, P., Speros, S.J., Bieg, S.  
**Lymphopenia in the BB rat model of type 1 diabetes is due to a mutation in a novel immune-associated nucleotide (*Ian*)-related gene**  
(2002) *Genome Res*, 12 (7), pp. 1029-1039.  
COI: 1:CAS:528:DC%2BD38XIsVWWhu7Y%3D, PID: 12097339
- Rutledge, E.A., Fuller, J.M., Van Yserloo, B., Moralejo, D.H., Ettinger, R.A., Gaur, P., Hoehna, J.L., Kwitek, A.E.  
**Sequence variation and expression of the *Gimap* gene family in the BB rat**  
(2009) *Exp Diabetes Res*, 2009.
- Miyamura, N., Amemiya, T.  
**Lens and retinal changes in the WBN/Kob rat (spontaneously diabetic strain)**  
(1998) *Ophthalmic Res*, 30 (4), pp. 221-232.  
COI: 1:STN:280:DyaK1czjtFKkug%3D%3D, PID: 9667053
- Mori, M., Fu, X., Chen, L., Zhang, G., Higuchi, K.  
**Hereditary pancreatitis model WBN/Kob rat strain has a unique haplotype in the *Pdwk1* region on chromosome 7**  
(2009) *Exp Anim*, 58 (4), pp. 409-413.  
COI: 1:CAS:528:DC%2BD1MXhtFchtLvK, PID: 19654439
- Kakehashi, A., Saito, Y., Mori, K., Sugi, N., Ono, R., Yamagami, H., Shinohara, M., Kanazawa, Y.  
**Characteristics of diabetic retinopathy in SDT rats**  
(2006) *Diabetes Metab Res Rev*, 22 (6), pp. 455-461.  
PID: 16572493
- Sasase, T., Ohta, T., Masuyama, T., Yokoi, N., Kakehashi, A., Shinohara, M.  
**The spontaneously diabetic torii rat: an animal model of nonobese type 2 diabetes with severe diabetic complications**  
(2013) *J Diabetes Res*, 2013, p. 976209.
- Shinohara, M., Masuyama, T., Shoda, T., Takahashi, T., Katsuda, Y., Komeda, K., Kuroki, M., Kanazawa, Y.  
**A new spontaneously diabetic non-obese Torii rat strain with severe ocular complications**  
(2000) *Int J Exp Diabetes Res*, 1 (2), pp. 89-100.  
COI: 1:STN:280:DC%2BD3MvhvFOjsA%3D%3D, PID: 11469401
- Yamada, H., Yamada, E., Higuchi, A., Matsumura, M.  
**Retinal neovascularisation without ischaemia in the spontaneously diabetic Torii rat**  
(2005) *Diabetologia*, 48 (8), pp. 1663-1668.  
COI: 1:STN:280:DC%2BD2MvivFGGsA%3D%3D, PID: 15977012
- Movassat, J., Calderari, S., Fernández, E., Martín, M.A., Escrivá, F., Plachot, C., Gangnerau, M.N., Portha, B.  
**Type 2 diabetes—a matter of failing  $\beta$ -cell neogenesis? Clues from the GK rat model**  
(2007) *Diabetes Obes Metab*, 9, pp. 187-195.  
COI: 1:CAS:528:DC%2BD2sXhtlOhsb%2FK, PID: 17919193
- Calderari, S., Gangnerau, M.N., Thibault, M., Meile, M.J., Kassis, N., Alvarez, C., Portha, B., Serradas, P.  
**Defective *IGF2* and *IGF1R* protein production in embryonic pancreas precedes beta**

**cell mass anomaly in the goto–kakizaki rat model of type 2 diabetes**

(2007) *Diabetologia*, 50, pp. 1463-1471.

COI: 1:CAS:528:DC%2BD2sXmtFektLg%3D, PID: 17476475

- Miyamoto, K., Ogura, Y., Nishiwaki, H., Matsuda, N., Honda, Y., Kato, S., Ishida, H., Seino, Y.  
**Evaluation of retinal microcirculatory alterations in the Goto-Kakizaki rat. A spontaneous model of non-insulin-dependent diabetes**  
(1996) *Invest Ophthalmol Vis Sci*, 37 (5), pp. 898-905.  
COI: 1:STN:280:DyaK287otFCntQ%3D%3D, PID: 8603874
- Han, Z., Guo, J., Conley, S.M., Naash, M.I.  
**Retinal angiogenesis in the Ins2Akita mouse model of diabetic retinopathy**  
(2013) *Invest Ophthalmol Vis Sci*, 54 (1), pp. 574-584.  
COI: 1:CAS:528:DC%2BC3sXjt1ertbk%3D, PID: 23221078
- Gastinger, M.J., Kunselman, A.R., Conboy, E.E., Bronson, S.K., Barber, A.J.  
**Dendrite remodeling and other abnormalities in the retinal ganglion cells of Ins2Akita diabetic mice**  
(2008) *Invest Ophthalmol Vis Sci*, 49 (6), pp. 2635-2642.  
PID: 18515593
- Li, C.R., Sun, S.G.  
**VEGF expression and cell apoptosis in NOD mouse retina**  
(2010) *Int J Ophthalmol*, 3 (3), pp. 224-227.  
PID: 22553559
- Zorrilla-Zubilete, M.A., Yeste, A., Quintana, F.J., Toiber, D., Mostoslavsky, R., Silberman, D.M.  
**Epigenetic control of early neurodegenerative events in diabetic retinopathy by the histone deacetylase SIRT 6**  
(2018) *J Neurochem*, 144 (2), pp. 128-138.  
COI: 1:CAS:528:DC%2BC2sXhvVeitb3O, PID: 29049850
- Lee, S., Harris, N.R.  
**Losartan and ozagrel reverse retinal arteriolar constriction in non-obese diabetic mice**  
(2008) *Microcirculation*, 15 (5), pp. 379-387.
- Shaw, S.G., Boden, J.P., Biecker, E., Reichen, J., Rothen, B.  
**Endothelin antagonism prevents diabetic retinopathy in NOD mice: a potential role of the angiogenic factor adrenomedullin**  
(2006) *Exp Biol Med*, 231 (6), pp. 1101-1105.  
COI: 1:CAS:528:DC%2BD28XIt1ertLc%3D
- Clements, R.S., Jr., Robison, W.G., Jr., Cohen, M.P.  
**Anti-glycated albumin therapy ameliorates early retinal microvascular pathology in db/db mice**  
(1998) *J Diabetes Complicat*, 12 (1), pp. 28-33.
- Ding, Y., Yuan, S., Liu, X., Mao, P., Zhao, C., Huang, Q., Zhang, R., Xie, P.  
**Protective effects of astragaloside IV on db/db mice with diabetic retinopathy**  
(2014) *PLoS ONE*, 9 (11).
- Cheung, A.K., Fung, M.K., Lo, A.C., Lam, T.T., So, K.F., Chung, S.S., Chung, S.K.  
**Aldose reductase deficiency prevents diabetes-induced blood-retinal barrier breakdown, apoptosis, and glial reactivation in the retina of db/db mice**  
(2005) *Diabetes*, 54 (11), pp. 3119-3125.  
COI: 1:CAS:528:DC%2BD2MXht1Siu7bL, PID: 16249434

- Bogdanov, P., Corraliza, L., Villena, A., Carvalho, J., Garcia-Arumi, A.R., Ramos, J., Ruberte, D., Hernandez, R.  
**The db/db mouse: a useful model for the study of diabetic retinal neurodegeneration**  
(2014) *PLoS ONE*, 9 (5).
- Samuels, I.S., Bell, B.A., Pereira, A., Saxon, J., Peachey, N.S.  
**Early retinal pigment epithelium dysfunction is concomitant with hyperglycemia in mouse models of type 1 and type 2 diabetes**  
(2015) *J Neurophysiol*, 113 (4), pp. 1085-1099.  
COI: 1:CAS:528:DC%2BC2MXkt12qtLw%3D, PID: 25429122
- van Eeden, P.E., Tee, L.B., Lukehurst, S., Lai, C.-M., Rakoczy, E.P., Beazley, L.D., Dunlop, S.A.  
**Early vascular and neuronal changes in a VEGF transgenic mouse model of retinal neovascularization**  
(2006) *Invest Ophthalmol Vis Sci*, 47 (10), pp. 4638-4645.  
PID: 17003462
- Shen, W.-Y., Lai, C.-M., Graham, C., Binz, N., Lai, Y., Eade, J., Guidolin, D., Rakoczy, P.  
**Long-term global retinal microvascular changes in a transgenic vascular endothelial growth factor mouse model**  
(2006) *Diabetologia*, 49 (7), pp. 1690-1701.  
COI: 1:CAS:528:DC%2BD28XIt1Ojurg%3D, PID: 16752188
- Wisniewska-Kruk, J., Klaassen, I., Vogels, I.M., Magno, A.L., Lai, C.-M., Van Noorden, C.J., Schlingemann, R.O., Rakoczy, E.P.  
**Molecular analysis of blood-retinal barrier loss in the Akimba mouse, a model of advanced diabetic retinopathy**  
(2014) *Exp Eye Res*, 122, pp. 123-131.  
COI: 1:CAS:528:DC%2BC2cXnsFCgsr4%3D, PID: 24703908
- Danis, R.P., Yang, Y.  
**Microvascular retinopathy in the Zucker diabetic fatty rat**  
(1993) *Invest Ophthalmol Vis Sci*, 34 (7), pp. 2367-2371.  
COI: 1:STN:280:DyaK3s3nvF2mug%3D%3D, PID: 8505219
- Kowluru, R.A., Mishra, M., Kowluru, A., Kumar, B.  
**Hyperlipidemia and the development of diabetic retinopathy: comparison between type 1 and type 2 animal models**  
(2016) *Metabolism*, 65 (10), pp. 1570-1581.  
COI: 1:CAS:528:DC%2BC28XhtIKqs73F, PID: 27621192
- Szabó, K., Énzsöly, A., Dékány, B., Szabó, A., Hajdú, R.I., Radovits, T., Mátyás, C., Merkely, B.  
**Histological evaluation of diabetic neurodegeneration in the retina of Zucker diabetic fatty (ZDF) rats**  
(2017) *Sci Rep*, 7 (1), p. 8891.
- Katsuda, Y., Ohta, T., Miyajima, K., Kemmochi, Y., Sasase, T., Tong, B., Shinohara, M., Yamada, T.  
**Diabetic complications in obese type 2 diabetic rat models**  
(2014) *Exp Anim*, 63 (2), pp. 121-132.  
COI: 1:CAS:528:DC%2BC2cXhtFaltLnK, PID: 24770637
- Behl, Y., Krothapalli, P., Desta, T., DiPiazza, A., Roy, S., Graves, D.T.  
**Diabetes-enhanced tumor necrosis factor- $\alpha$  production promotes apoptosis and the loss of retinal microvascular cells in type 1 and type 2 models of diabetic retinopathy**  
(2008) *Am J Pathol*, 172 (5), pp. 1411-1418.  
PID: 18403591

- Wohlfart, P., Lin, J., Dietrich, N., Kannt, A., Elvert, R., Herling, A.W., Hammes, H.P.  
**Expression patterning reveals retinal inflammation as a minor factor in experimental retinopathy of ZDF rats**  
(2014) *Acta Diabetol*, 51, pp. 553-558.  
COI: 1:CAS:528:DC%2BC2cXhtlamsLvK, PID: 24477469
- Bhutto, I.A., Lu, Z.-Y., Takami, Y., Amemiya, T.  
**Retinal and choroidal vasculature in rats with spontaneous diabetes type 2 treated with the angiotensin-converting enzyme inhibitor cilazapril: corrosion cast and electron-microscopic study**  
(2002) *Ophthalmic Res*, 34 (4), pp. 220-231.  
COI: 1:CAS:528:DC%2BD38Xnt1Oiu7o%3D, PID: 12297695
- Shirao, Y., Kawasaki, K.  
**Electrical responses from diabetic retina**  
(1998) *Prog Retin Eye Res*, 17, pp. 59-76.  
COI: 1:STN:280:DyaK1c7nsl2jsw%3D%3D, PID: 9537795
- Matsuura, T., Yamagishi, S., Kodama, Y., Shibata, R., Ueda, S., Narama, I.  
**Otsuka Long-Evans Tokushima fatty (OLETF) rat is not a suitable animal model for the study of angiopathic diabetic retinopathy**  
(2005) *Int J Tissue React*, 27 (2), pp. 59-62.  
COI: 1:STN:280:DC%2BD2MzmvVWgtg%3D%3D, PID: 16035649
- Sima, A.A., Bouchier, M., Christensen, H.  
**Axonal atrophy in sensory nerves of the diabetic BB-Wistar rat: a possible early correlate of human diabetic neuropathy**  
(1983) *Ann Neurol*, 13 (3), pp. 264-272.  
COI: 1:STN:280:DyaL3s3gt1OnsA%3D%3D, PID: 6847138
- Sima, A.A., Chakrabarti, S., Garcia-Salinas, R., Basu, P.K.  
**The BB-rat-an authentic model of human diabetic retinopathy**  
(1985) *Curr Eye Res*, 4 (10), pp. 1087-1092.  
COI: 1:STN:280:DyaL28%2FIsV2juw%3D%3D, PID: 4064731
- Robinson, W.G., McCaleb, M.L., Feld, L.G., Michaelis, O.E., And, N.L., Mercandetti, M.  
**Degenerated intramural pericytes ('ghost cells') in the retinal capillaries of diabetic rats**  
(1991) *Curr Eye Res*, 10 (4), pp. 339-350.
- Blair, N.P., Tso, M.O., Dodge, J.T.  
**Pathologic studies of the blood-retinal barrier in the spontaneously diabetic BB rat**  
(1984) *Invest Ophthalmol Vis Sci*, 25 (3), pp. 302-311.  
COI: 1:STN:280:DyaL2c7jsV2gsw%3D%3D, PID: 6698748
- Miyamura, N., Amemiya, T.  
**Lens and retinal changes in the WBN/Kob rat (spontaneously Diabetic strain) Electron-microscopic study**  
(1998) *Ophthal Res*, 30 (4), pp. 221-232.  
COI: 1:STN:280:DyaK1czjtFKkug%3D%3D
- Tsuji, N., Matsuura, T., Ozaki, K., Sano, T., Narama, I.  
**Diabetic retinopathy and choroidal angiopathy in diabetic rats (WBN/Kob)**  
(2009) *Exp Anim*, 58 (5), pp. 481-487.  
COI: 1:CAS:528:DC%2BC3cXjsFGjt74%3D, PID: 19897931
- Matsuura, T., Horikiri, K., Ozaki, K., Narama, I.  
**Proliferative retinal changes in diabetic rats (WBN/Kob)**  
(1999) *Comp Med*, 49 (5), pp. 565-569.  
COI: 1:STN:280:DC%2BD3c%2FhslKhsA%3D%3D



- Ogawa, T., Ohira, A., Amemiya, T.  
**Superoxide dismutases in retinal degeneration of WBN/Kob rat**  
(1998) *Curr Eye Res*, 17 (11), pp. 1067-1073.  
COI: 1:STN:280:DyaK1M%2FmtFSrsA%3D%3D, PID: 9846625
- Fukuda, M., Nakanishi, Y., Fuse, M., Yokoi, N., Hamada, Y., Fukagawa, M., Negi, A., Nakamura, M.  
**Altered expression of aquaporins 1 and 4 coincides with neurodegenerative events in retinas of spontaneously diabetic Torii rats**  
(2010) *Exp Eye Res*, 90 (1), pp. 17-25.  
COI: 1:CAS:528:DC%2BD1MXhsFantbjP, PID: 19748503
- Matsuoka, M., Ogata, N., Minamino, K., Matsumura, M.  
**Leukostasis and pigment epithelium-derived factor in rat models of diabetic retinopathy**  
(2007) *Mol Vis*, 13, p. 1058.  
COI: 1:CAS:528:DC%2BD2sXptlKmtLc%3D, PID: 17653050
- Sasase, T., Morinaga, H., Abe, T., Miyajima, K., Ohta, T., Shinohara, M., Matsushita, M., Kakehashi, A.  
**Protein kinase C beta inhibitor prevents diabetic peripheral neuropathy, but not histopathological abnormalities of retina in spontaneously Diabetic Torii rat**  
(2009) *Diabetes Obes Metab*, 11 (11), pp. 1084-1087.  
COI: 1:CAS:528:DC%2BD1MXhtl2ktbrO, PID: 19614949
- Carmo, A., Cunha-Vaz, J., Carvalho, A., Lopes, M.  
**Nitric oxide synthase activity in retinas from non-insulin-dependent diabetic Goto-Kakizaki rats: correlation with blood-retinal barrier permeability**  
(2000) *Nitric Oxide*, 4 (6), pp. 590-596.  
COI: 1:CAS:528:DC%2BD3MXnsVak, PID: 11139367
- Yatoh, S., Mizutani, M., Yokoo, T., Kozawa, T., Sone, H., Toyoshima, H., Suzuki, S., Yamada, N.  
**Antioxidants and an inhibitor of advanced glycation ameliorate death of retinal microvascular cells in diabetic retinopathy**  
(2006) *Diabetes Metab Res Rev*, 22 (1), pp. 38-45.  
COI: 1:CAS:528:DC%2BD28Xhs1Kku7c%3D, PID: 15892182
- Berdugo, M., Delaunay, K., Lebon, C., Naud, M.C., Radet, L., Zennaro, L., Picard, E., Polak, M.  
**Long-term oral treatment with non-hypoglycemic dose of glibenclamide reduces diabetic retinopathy damage in the goto-kakizaki rat model**  
(2021) *Pharmaceutics*, 13 (7), p. 1095.
- Gong, C.Y., Lu, B., Sheng, Y.C., Yu, Z.Y., Zhou, J.Y., Ji, L.L.  
**The development of diabetic retinopathy in Goto-Kakizaki rat and the expression of angiogenesis-related signals**  
(2016) *Chin J Physiol*, 59 (2), pp. 100-108.  
COI: 1:CAS:528:DC%2BC1cXmsVyhtrk%3D, PID: 27080465
- Hachana, S., Pouliot, M., Couture, R., Vaucher, E.  
**Diabetes-induced inflammation and vascular alterations in the goto-kakizaki rat retina**  
(2020) *Curr Eye Res*, 45 (8), pp. 965-974.  
PID: 31902231
- Kim, M.K., Kim, S.G., Lee, S.K.  
**4-Hexylresorcinol-induced angiogenesis potential in human endothelial cells**  
(2020) *Maxillofac Plast Reconstr Surg*, 42 (1), pp. 1-11.

- Durham, J.T., Dulmovits, B.M., Cronk, S.M., Sheets, A.R., Herman, I.M.  
**Pericyte chemomechanics and the angiogenic switch: insights into the pathogenesis of proliferative diabetic retinopathy?**  
(2015) *Invest Ophthalmol Vis Sci*, 56 (6), pp. 3441-3459.  
COI: 1:CAS:528:DC%2BC28XntV2ru7Y%3D, PID: 26030100
- Gong, Y., Fu, Z., Edin, M.L., Liu, C.-H., Wang, Z., Shao, Z., Fredrick, T.W., Burnim, S.B.  
**Cytochrome P450 oxidase 2 C inhibition adds to  $\omega$ -3 long-chain polyunsaturated fatty acids protection against retinal and choroidal neovascularization**  
(2016) *Arterio Thromb Vasc Biol*, 36 (9), pp. 1919-1927.  
COI: 1:CAS:528:DC%2BC28Xhtl2msLnM
- Yu, Z., Zhang, T., Gong, C., Sheng, Y., Lu, B., Zhou, L., Ji, L., Wang, Z.  
**Erianin inhibits high glucose-induced retinal angiogenesis via blocking ERK1/2-regulated HIF-1 $\alpha$ -VEGF/VEGFR2 signaling pathway**  
(2016) *Sci Rep*, 6 (1), pp. 1-15.
- Johnen, S., Djalali-Talab, Y., Kazanskaya, O., Möller, T., Harmening, N., Kropp, M., Izsvák, Z., Thumann, G.  
**Antiangiogenic and neurogenic activities of sleeping Beauty-mediated PEDF-transfected RPE cells in vitro and in vivo**  
(2015) *BioMed Res Int*, 2015, p. 863845.
- Spuul, P., Daubon, T., Pitter, B., Alonso, F., Fremaux, I., Kramer, I., Montanez, E., Génot, E.  
**VEGF-A/Notch-induced podosomes proteolyse basement membrane collagen-IV during retinal sprouting angiogenesis**  
(2016) *Cell Rep*, 17 (2), pp. 484-500.  
COI: 1:CAS:528:DC%2BC28Xhs1aksb%2FJ, PID: 27705796
- Siemerink, M.J., Hughes, M.R., Dallinga, M.G., Gora, T., Cait, J., Vogels, I.M., Yetin-Arik, B., McNagny, K.M.  
**CD34 promotes pathological epi-retinal neovascularization in a mouse model of oxygen-induced retinopathy**  
(2016) *PLoS ONE*, 11 (6).  
PID: 27352134
- Bergers, G., Song, S.  
**The role of pericytes in blood-vessel formation and maintenance**  
(2005) *Neuro Oncol*, 7 (4), pp. 452-464.  
COI: 1:CAS:528:DC%2BD2MXht1SisLvP, PID: 16212810
- Yanni, S.E., Clark, M.L., Yang, R., Bingaman, D.P., Penn, J.S.  
**The effects of nepafenac and amfenac on retinal angiogenesis**  
(2010) *Brain Res Bull*, 81 (2-3), pp. 310-319.  
COI: 1:CAS:528:DC%2BC3cXkt1CrtA%3D%3D, PID: 19897019
- Moleiro, A., Conceição, G., Leite-Moreira, A., Rocha-Sousa, A.  
**A critical analysis of the available in vitro and ex vivo methods to study retinal angiogenesis**  
(2017) *J Ophthalmol*, 2017.
- Rezzola, S., Belleri, M., Ribatti, D., Costagliola, C., Presta, M., Semeraro, F.  
**A novel ex vivo murine retina angiogenesis (EMRA) assay**  
(2013) *Exp Eye Res*, 112, pp. 51-56.  
COI: 1:CAS:528:DC%2BC3sXhtVWIs73E, PID: 23631846
- Schnichels, S., Paquet-Durand, F., Löscher, M., Tsai, T., Hurst, J., Joachim, S.C., Klettner, A.  
**Retina in a dish: cell cultures, retinal explants and animal models for common diseases of the retina**

(2021) *Prog Retin Eye Res*, 81, p. 100880.

COI: 1:CAS:528:DC%2BB3cXhsl2kt7%2FM, PID: 32721458

- Lücke, M., Januschowski, K., Lücke, J., Peters, S., Wirtz, N., Yörük, E., Lücke, C., Szurman, P.  
**The effects of ranibizumab (Lucentis) on retinal function in isolated perfused vertebrate retina**  
(2009) *Br J Ophthalmol*, 93 (10), pp. 1396-1400.  
PID: 19628500
- Forrester, J.V., Chapman, A., Kerr, C., Roberts, J., Lee, W.R., Lackie, J.M.  
**Bovine retinal explants cultured in collagen gels: a model system for the study of proliferative retinopathy**  
(1990) *Arch Ophthalmol*, 108 (3), pp. 415-420.  
COI: 1:STN:280:DyaK3c7nvFGmuw%3D%3D, PID: 2106871
- Nowak-Sliwinska, P., Alitalo, K., Allen, E., Anisimov, A., Aplin, A.C., Auerbach, R., Augustin, H.G., Bergers, G.  
**Consensus guidelines for the use and interpretation of angiogenesis assays**  
(2018) *Angiogenesis*, 21, pp. 425-532.  
PID: 29766399
- Alarautalahti, V., Ragauskas, S., Hakkarainen, J.J., Uusitalo-Järvinen, H., Uusitalo, H., Hyttinen, J., Kalesnykas, G., Nymark, S.  
**Viability of mouse retinal explant cultures assessed by preservation of functionality and morphology**  
(2019) *Invest Ophthalmol Vis Sci*, 60 (6), pp. 1914-1927.  
COI: 1:CAS:528:DC%2BC1MXit1Cit7zF, PID: 31042799
- Murakami, T., Suzuma, K., Takagi, H., Kita, M., Ohashi, H., Watanabe, D., Ojima, T., Sakamoto, A.  
**Time-lapse imaging of vitreoretinal angiogenesis originating from both quiescent and mature vessels in a novel ex vivo system**  
(2006) *Invest Ophthalmol Vis Sci*, 47 (12), pp. 5529-5536.  
PID: 17122145
- Amato, R., Biagioni, M., Cammalleri, M., Dal Monte, M., Casini, G.  
**VEGF as a survival factor in ex vivo models of early diabetic retinopathy**  
(2016) *Invest Ophthalmol Vis Sci*, 57 (7), pp. 3066-3076.  
COI: 1:CAS:528:DC%2BC28XhsVyrbtzL, PID: 27286364
- Chantelau, E., Meyer-Schwickerath, R., Klabe, K.  
**Downregulation of serum IGF-1 for treatment of early worsening of diabetic retinopathy: a long-term follow-up of two cases**  
(2010) *Ophthalmol*, 224 (4), pp. 243-246.
- Haurigot, V., Villacampa, P., Ribera, A., Bosch, A., Ramos, D., Ruberte, J., Bosch, F.  
**Long-term retinal PEDF overexpression prevents neovascularization in a murine adult model of retinopathy**  
(2012) *PLoS ONE*, 7 (7).  
COI: 1:CAS:528:DC%2BC38XhtFSkt77M, PID: 22911805
- Simo, R., Carrasco, E., Garcia-Ramirez, M., Hernandez, C.  
**Angiogenic and antiangiogenic factors in proliferative diabetic retinopathy**  
(2006) *Curr Diabetes Rev*, 2 (1), pp. 71-98.  
COI: 1:CAS:528:DC%2BD28XjtVGjtLw%3D, PID: 18220619
- Whitmire, W., Al-Gayyar, M.M., Abdelsaid, M., Yousufzai, B.K., El-Remessy, A.B.  
**Alteration of growth factors and neuronal death in diabetic retinopathy: what we have learned so far**

(2011) *Mol Vis*, 17, p. 300.

PID: 21293735

- Sawamiphak, S., Ritter, M., Acker-Palmer, A.  
**Preparation of retinal explant cultures to study ex vivo tip endothelial cell responses**  
(2010) *Nat Protoc*, 5 (10), pp. 1659-1665.  
COI: 1:CAS:528:DC%2BC3cXht1agsbvl, PID: 20885378
- Sadikan, M.Z., Abdul Nasir, N.A.  
**Diabetic retinopathy: Emerging concepts of current and potential therapy**  
(2023) *Naunyn Schmiedebergs Arch Pharmacol*, pp. 1-12.
- Sadikan, M.Z., Nasir, N.A.A., Ghani, N.A.A., Lambuk, L., Iezhitsa, I.N., Agarwal, R.  
**The Use of Fiji Image J as an Image Analysis Tool for Measuring Retinal Vessel Diameter in Rodent Model of Diabetic Retinopathy**  
(2021) *Asian J Med Biomed*, 5 (1), pp. 61-66.
- Abdul Ghani, N.A., Abdul Nasir, N.A., Lambuk, L., Sadikan, M.Z., Agarwal, R., Ramli, N.  
**The effect of palm oil-derived tocotrienol-rich fraction in preserving normal retinal vascular diameter in streptozotocin-induced diabetic rats**  
(2023) *Graefes Arch Clin Exp Ophthalmol*, 261 (6), pp. 1587-1596.  
(,); -,., <https://doi.org/10.1007/s00417-022-05965-3>
- Sadikan, M.Z., Abdul Nasir, N.A., Agarwal, R., Mohd Ismail, N.  
**Protective effect of palm oil-derived tocotrienol-rich fraction against retinal neurodegenerative changes in rats with streptozotocin-induced diabetic retinopathy**  
(2020) *Biomolecules*, 10 (4), p. 556.  
<https://doi.org/10.3390/biom10040556>

#### Correspondence Address

Abdul Nasir N.A.; Centre for Neuroscience Research (NeuRon), Selangor, Malaysia; email: [nurulalimah@uitm.edu.my](mailto:nurulalimah@uitm.edu.my)

**Publisher:** BioMed Central Ltd

**ISSN:** 14712415

**PubMed ID:** 37858128

**Language of Original Document:** English

**Abbreviated Source Title:** BMC Ophthalmol.

2-s2.0-85174484154

**Document Type:** Review

**Publication Stage:** Final

**Source:** Scopus

**ELSEVIER**

Copyright © 2023 Elsevier B.V. All rights reserved. Scopus® is a registered trademark of Elsevier B.V.

 RELX Group™