|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter** | | | **How to get** | **Status** |
| Geometry | Adipocyte | Diameter of one cell | Search | O |
| Surface area of one cell | Calculate | - |
| Volume of one cell | Calculate | - |
| Total surface areas of adipocytes | Calculate | - |
| The number of adipocytes | Search | O |
| Macrophage | Diameter of one cell | Search | O |
| Surface area of one cell | Calculate | - |
| Volume of one cell | Calculate | - |
| Total surface areas of macrophages | Calculate | - |
| The number of macrophages | Search |  |
| Capillary | Cross-sectional area of one microvessel | Search | O |
| Perimeter of one microvessel | Search | O |
| Outer diameter of one microvessel | Calculate | - |
| Capillary-adipocyte ratio | Search | O |
| Capillary density | Search | O |
| Total surface area of microvessels | Calculate | - |
| Endothelial cell thickness | Search | O |
| Surface areas of one endothelial cell | Search | O |
| Total blood volume | Search | X |
| Interstitial space | Capillary basement membrane (CBM) thickness | Search | Δ |
| Adipocyte basement membrane (ABM) thickness | Search | Δ |
| Extracellular fluid or interstitial fluid volume fraction | Search | O |
| Non-fluid components volume fraction in CBM | Search | O |
| Non-fluid components volume fraction in ABM | Search | O |
| Non-fluid components volume fraction in extracellular matrix (ECM) | Search | O |
| Size of pore in CBM | Search | Δ |
| Size of pore in ABM | Search | Δ |
| Kinetics | VEGF-A | VEGF-A binding to VEGFR1 | Check cited literature | O |
| VEGF-A binding to VEGFR2 | Check cited literature | O |
| VEGF-A binding to NRP1 | Check cited literature | O |
| VEGF-A binding to NRP2 | Check cited literature | O |
| VEGF-A binding to GAGs | Check cited literature | O |
| VEGF-B | VEGF-B binding to VEGFR1 | Search | O |
| VEGF-B binding to NRP1 | Search | O |
| VEGF-B binding to GAGs | Search | O |
| Receptors | Coupling of NRP1 and VEGFR1 | Check cited literature | O |
| Coupling of NRP1/2 and VEGFR2 | Check cited literature | Δ |
| VEGFR internalization | Check cited literature | O |
| Binding site densities | | ECM | Check cited literature | O |
| CBM | Check cited literature | O |
| ABM | Check cited literature | O |
| Transport | | VEGF-165 secretion rate | Tuned | X |
| VEGF-121 secretion rate | Tuned | X |
| VEGF-B secretion rate | Tuned | X |
| VEGF clearance | Check cited literature | O |
| VEGF degradation | Check cited literature | O |

* **Adipocyte size (mean diameter)**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Strain** | **Sex** | **n** | **Age** | **Diet** | **Duration of diet** | **Body weight** | **Location** | **Method** | **Value** |
| (Lijnen et al., 2006) | Mouse | Swiss × 129SV | Male | 15 | 20 wk. | SFD | 15 wk. | 38±1.4 g | Gonadal fat | Computer-assisted image analysis | 44.99 µm  [42.37, 47.47] |
| Male | 10 | HFD | 57±1.4 g | 65.80 µm  [63.93, 67.61] |
| (Lijnen et al., 2001) | Mouse | C57/Bl6 × 129SVj | Both | ? | 22 wk. | SFD | 17 wk. | 27±2.2 g | Gonadal fat | Computer-assisted image analysis | 49±4.2 µm |
| Both | ? | HFD | 39±3.1 g | 80±5.3 µm |
| Both | ? | 37 wk. | HFD | 32 wk. | 39±2.2 g | 86±1.6 µm |
| (Maquoi et al., 2002) | Mouse | C57/Bl6 × 129SVj | Male | 2 | 20 wk. | SFD | 15 wk. | 28±1.2 g | Gonadal fat | Computer-assisted image analysis | 42 µm |
| Male | 6 | HFD | 40±1.4 g | 83±3 µm |
| (Morange et al., 2000) | Mouse | C57BL/6 × 129SV | Both | 7 to 11 | 21 wk. | SFD | 17 wk. | 28±1.4 g | Gonadal fat | Computer-assisted image analysis | 49±4.3 µm |
| Both | 7 to 11 | HFD | 42±2 g | 82±3.5 µm |
| (Voros et al., 2005) | Mouse | C57Bl/6 | Male | ? | 7 wk. | SFD | 2 wk. | 21.1±0.7 g | Gonadal fat | Computer-assisted image analysis | 21.41±0.83 µm |
| Male | ? | HFD | 26.4±0.6 g | 34.6±0.72 µm |
| Male | ? | 10 wk. | SFD | 5 wk. | 25.4±0.4 g | 26.94±0.47 µm |
| Male | ? | HFD | 32.9±0.9 g | 40.68±2.03 µm |
| Male | ? | 20 wk. | SFD | 15 wk. | 30.0±0.62 g | 28.77±1.06 µm |
| Male | ? | HFD | 46.3±1.77 g | 52.93±0.46 µm |
| (Lijnen, Maquoi, et al., 2003) | Mouse | C57/Bl6 | Male | 12 to 20 | 20 wk. | SFD | 15 wk. | 33±0.91 g | Gonadal fat | Computer-assisted image analysis | 62±4.1 µm |
| Male | 12 to 20 | HFD | 45±1.4 g | 85±2.3 µm |
| (Lijnen, Demeulemeester, et al., 2003) | Mouse | C57Bl/6 × 129 SvJae | Male | 4 | 20 wk. | SFD | 15 wk. | 29.4±0.6 g | Gonadal fat | Computer-assisted image analysis | 40.05±0.76 µm |
| Male | 10 | HFD | 41±1.8 g | 94.61±4.58 µm |
| (Maquoi et al., 2003) | Mouse | B10.RIII | Male | 11 | 20 wk. | HFD | 15 wk. | 37±1.5 g | Gonadal fat | Computer-assisted image analysis | 76.36±2.25 µm |
| (Lijnen et al., 2007) | Mouse | C57Bl/6 | Male | 8 | 20 wk. | HFD | 15 wk. | 42±1.4 g | Gonadal fat | Computer-assisted image analysis | 89.13±1.46 µm |
| (Van Hul et al., 2012) | Mouse | C57Bl6/129SvJ/EMS + Ter | Male | 10 to 14 | 20 wk. | SFD | 15 wk. | 23±0.46 g | Gonadal fat | Computer-assisted image analysis | 42.4±1.95 µm |
| 10 to 14 | HFD | 27±0.72 g | 58.37±2.22 µm |

\* [,] shows minimum and maximum value.

* **The number of adipocytes**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Strain** | **Sex** | **n** | **Age** | **Diet** | **Duration of diet** | **Body weight** | **Location** | **Method** | **Value** |
| (Lijnen et al., 2001) | Mouse | C57/Bl6 × 129SVj | Both | ? | 22 wk. | SFD | 17 wk. | 27±2.2 g | Gonadal fat | Computer-assisted image analysis |  |
| Both | ? | HFD | 39±3.1 g |  |
| (Morange et al., 2000) | Mouse | C57BL/6 × 129SV | Both | 7 to 11 | 21 wk. | SFD | 17 wk. | 28±1.4 g | Gonadal fat | Computer-assisted image analysis |  |
| Both | 7 to 11 | HFD | 42±2 g |  |
| (Lijnen, Maquoi, et al., 2003) | Mouse | C57/Bl6 | Male | 12 to 20 | 20 wk. | SFD | 15 wk. | 33±0.91 g | Gonadal fat | Computer-assisted image analysis |  |
| Male | 12 to 20 | HFD | 45±1.4 g |  |

* **Weight of gonadal adipose tissue**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Strain** | **Sex** | **n** | **Age** | **Diet** | **Duration of diet** | **Body weight** | **Location** | **Method** | **Value** |
| (Lijnen et al., 2006) | Mouse | Swiss × 129SV | Male | 15 | 20 wk. | SFD | 15 wk. | 38±1.4 g | Gonadal fat | Computer-assisted image analysis | 1.05±0.12 g |
| Male | 10 | HFD | 57±1.4 g | 1.74±0.068 g |
| (Lijnen et al., 2001) | Mouse | C57/Bl6 × 129SVj | Both | ? | 22 wk. | SFD | 17 wk. | 27±2.2 g | Gonadal fat | Computer-assisted image analysis | 0.34±0.09 g |
| HFD | 39±3.1 g | 2.3±0.43 g |
| 37 wk. | SFD | 32 wk. | 26±2.8 g | 0.55±0.23 g |
| HFD | 39±2.2 g | 2.4±0.58 g |
| (Maquoi et al., 2002) | Mouse | C57/Bl6 × 129SVj | Male | 2 | 20 wk. | SFD | 15 wk. | 28±1.2 g | Gonadal fat | Computer-assisted image analysis | 0.31±0.04 g |
| Male | 6 | HFD | 40±1.4 g | 2.0±0.18 g |
| (Morange et al., 2000) | Mouse | C57BL/6 × 129SV | Both | 7 to 11 | 21 wk. | SFD | 17 wk. | 28±1.4 g | Gonadal fat | Computer-assisted image analysis | 0.42±0.1 g |
| Both | 7 to 11 | HFD | 42±2 g | 1.9±0.2 g |
| (Voros et al., 2005) | Mouse | C57Bl/6 | Male | ? | 7 wk. | SFD | 2 wk. | 21.1±0.7 g | Gonadal fat | Computer-assisted image analysis | 0.18±0.018 g |
| Male | ? | HFD | 26.4±0.6 g | 0.28±0.019 g |
| Male | ? | 10 wk. | SFD | 5 wk. | 25.4±0.4 g | 0.59±0.094 g |
| Male | ? | HFD | 32.9±0.9 g | 0.67±0.044 g |
| Male | ? | 20 wk. | SFD | 15 wk. | 30.0±0.62 g | 1.2±0.093 g |
| Male | ? | HFD | 46.3±1.77 g | 1.6±0.062 g |
| (Lijnen, Maquoi, et al., 2003) | Mouse | C57/Bl6 | Male | 12 to 20 | 20 wk. | SFD | 15 wk. | 33±0.91 g | Gonadal fat | Computer-assisted image analysis | 0.49±0.073 g |
| Male | 12 to 20 | HFD | 45±1.4 g | 1.62±0.15 g |
| (Lijnen, Demeulemeester, et al., 2003) | Mouse | C57Bl/6 × 129 SvJae | Male | 4 | 20 wk. | SFD | 15 wk. | 29.4±0.6 g | Gonadal fat | Computer-assisted image analysis | 0.29±0.035 g |
| Male | 10 | HFD | 41±1.8 g | 1.85±0.18 g |
| (Maquoi et al., 2003) | Mouse | B10.RIII | Male | 11 | 20 wk. | HFD | 15 wk. | 37±1.5 g | Gonadal fat | Computer-assisted image analysis | 1.4±0.13 g |
| (Lijnen et al., 2007) | Mouse | C57Bl/6 | Male | 8 | 20 wk. | HFD | 15 wk. | 42±1.4 g | Gonadal fat | Computer-assisted image analysis | 2.38±0.14 g |
| (Van Hul et al., 2012) | Mouse | C57Bl6/129SvJ/EMS + Ter | Male | 10 to 14 | 20 wk. | SFD | 15 wk. | 23±0.46 g | Gonadal fat | Computer-assisted image analysis | 0.224±0.025 g |
| 10 to 14 | HFD | 27±0.72 g | 0.842±0.097 g |

* **Macrophage size**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Strain** | **Sex** | **n** | **Age** | **Diet** | **Body weight** | **Location** | **Method** | **Diameter** | **Volume** |
| (Krombach et al., 1997) | Rat | Sprague Dawley | Male | 12 | ? | SFD *ad libitum* | 250-350 g | Lung | 1. Harvest alveolar macrophage using bronchoalveolar lavage. 2. Measure the cell size using flow cytometric analysis. | 13.1±0.2 µm | 1166.0±41.5 µm3 |
| Hamster | Syrian golden | Male | 8 | ? | SFD *ad libitum* | 120-150 g | 13.6±0.4 µm | 1327.8±123.4 µm3 |
| Monkey | Adult cynomolgus | Both | 7 | ? | *ad libitum* | 3.5-7.0 kg | 15.5±0.5 µm | 1926.4±193.1 µm3 |
| Human | Non-smoking | Male | 10 | 25.6±1.2 y. | - | ? | 21.2±0.3 µm | 4989.9±174.0 µm3 |
| (Haley et al., 1991) | Mouse | B6C3F1 | Male | 4 | 10 wk. | *ad libitum* | ? | Lung | 1. Lavage alveolar macrophage using fiberoptic bronchoscope. 2. Centrifuge in a Shandon, Cytospin 2 cytocentrifuge 3. Use image analysis to measure the cell size. | 19±0.08 µm | ? |
| Rat | F344/Cr1 | Male | 4 | 10 wk. | *ad libitum* | ? | 18±0.08 µm | ? |
| Dog | Beagle | Male | 4 | 2 y. | *ad libitum* | ? | 16±0.09 µm | ? |
| Monkey | Cynomolgus | Male | 4 | ? | *ad libitum* | ? | 23±0.11 µm | ? |
| Chimpanzee | - | Male | 4 | 10 y. | *ad libitum* | ? | 23±0.11 µm | ? |
| Human | Non-smoking | Male | 4 | 24-34 y. | - | ? | 26±0.14 µm | ? |

* **Fibroblast size**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Sex** | **n** | **Age** | **Location** | **Method** | **Condition** | **Surface area** | **Volume** |
| (Kotaru et al., 2006) | Human | Both | 6 | Average 39 yr. | Airway (Lung) | Light microscopy | - | 2167±334 µm2 | ? |
| 6 | Distal lung | 937±72 µm2 | ? |
| (Thoumine et al., 1999) | Chick embryo | ? | 16 | 10 days | Heart | 1. Measure 1) the cell height, 2) the diameter of conjugation between the cell and microplate, and 3) the contact angle. 2. Fit theoretical equations to estimate cell surface and volume | Suspended-control | 735±120 µm2 | 1825±450 µm3 |
| 5 | Suspended-3h | 725±110 µm2 | 1790±400 µm3 |
| 12 | Suspended-cyt D | 640±140 µm2 | 1550±520 µm3 |
| 16 | Adherent | 760±130 µm2 | 1730±430 µm3 |
| 15 | Spread-0.5 h | 880±400 µm2 | 1750±680 µm3 |
| 15 | Spread-3 h | 1090±400 µm2 | 1600±650 µm3 |

* **Blood vessel size (cross-sectional area)**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Strain** | **Sex** | **n** | **Age** | **Diet** | **Duration of diet** | **Body weight** | **Location** | **Method** | **Value** |
| (Lijnen et al., 2006) | Mouse | Swiss × 129SV | Male | 15 | 20 wk. | SFD | 15 wk. | 38±1.4 g | Gonadal fat | Computer-assisted image analysis | 27±1.7 |
| Male | 10 | HFD | 57±1.4 g | 41±3.1 |
| (Voros et al., 2005) | Mouse | C57Bl/6 | Male | 5 | 7 wk. | SFD | 2 wk. | 21.1±0.7 g | Gonadal fat | Computer-assisted image analysis | 52±1.9 µm2 |
| Male | 5 | HFD | 26.4±0.6 g | 48±2.2 µm2 |
| Male | 5 | 10 wk. | SFD | 5 wk. | 25.4±0.4 g | 50±2.6 µm2 |
| Male | 5 | HFD | 32.9±0.9 g | 41±1.8 µm2 |
| Male | 5 | 20 wk. | SFD | 15 wk. | 30.0±0.62 g | 49±3.4 |
| Male | 5 | HFD | 46.3±1.77 g | 54±3.3 |
| (Lijnen, Maquoi, et al., 2003) | Mouse | C57/Bl6 | Male | 5 to 10 | 20 wk. | SFD | 15 wk. | 33±0.91 g | Gonadal fat | Computer-assisted image analysis | 74±4.8 |
| Male | 5 to 10 | HFD | 45±1.4 g | 140±19 |
| (Lijnen, Demeulemeester, et al., 2003) | Mouse | C57Bl/6 × 129 SvJae | Male | 4 | 20 wk. | SFD | 15 wk. | 29.4±0.6 g | Gonadal fat | Computer-assisted image analysis | ? |
| Male | 10 | HFD | 41±1.8 g | 47±2.6 |
| (Maquoi et al., 2003) | Mouse | B10.RIII | Male | 7 to 11 | 20 wk. | HFD | 15 wk. | 37±1.5 g | Gonadal fat | Computer-assisted image analysis | 76±3.9 |
| (Lijnen et al., 2007) | Mouse | C57Bl/6 | Male | 8 | 20 wk. | HFD | 15 wk. | 42±1.4 g | Gonadal fat | Computer-assisted image analysis | 108±7.7 |
| (Van Hul et al., 2012) | Mouse | C57Bl6/129SvJ/EMS + Ter | Male | 10 to 14 | 20 wk. | SFD | 15 wk. | 23±0.46 g | Gonadal fat | Computer-assisted image analysis | 59±5.1 |
| 10 to 14 | HFD | 27±0.72 g | 49±2.8 |

* **Blood vessel density (cross-sectional area)**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Strain** | **Sex** | **n** | **Age** | **Diet** | **Duration of diet** | **Body weight** | **Location** | **Method** | **Value** |
| (Lijnen et al., 2006) | Mouse | Swiss × 129SV | Male | 15 | 20 wk. | SFD | 15 wk. | 38±1.4 g | Gonadal fat | Computer-assisted image analysis | 370±37 |
| Male | 10 | HFD | 57±1.4 g | 290±23 |
| (Voros et al., 2005) | Mouse | C57Bl/6 | Male | 5 | 7 wk. | SFD | 2 wk. | 21.1±0.7 g | Gonadal fat | Computer-assisted image analysis | 1200±55/mm2 |
| Male | 5 | HFD | 26.4±0.6 g | 790±30/mm2 |
| Male | 5 | 10 wk. | SFD | 5 wk. | 25.4±0.4 g | 850±40/mm2 |
| Male | 5 | HFD | 32.9±0.9 g | 410±20/mm2 |
| Male | 5 | 20 wk. | SFD | 15 wk. | 30.0±0.62 g | 790±41 |
| Male | 5 | HFD | 46.3±1.77 g | 490±19 |
| Wild-type littermate of ob/ob | Male | 5 | ? | SFD | ? | 27±0.62 g | 830±87/mm2 |
| ob/ob | Male | 5 | 9 wk. | SFD | ? | 41±1.2 g | 390±21/mm2 |
| (Lijnen, Maquoi, et al., 200(L | Mouse | C57/Bl6 | Male | 5 to 10 | 20 wk. | SFD | 15 wk. | 33±0.91 g | Gonadal fat | Computer-assisted image analysis | 280±56 |
| Male | 5 to 10 | HFD | 45±1.4 g | 200±34 |
| (Lijnen, Demeulemeester, et al., 2003) | Mouse | C57Bl/6 × 129 SvJae | Male | 4 | 20 wk. | SFD | 15 wk. | 29.4±0.6 g | Gonadal fat | Computer-assisted image analysis | ? |
| Male | 10 | HFD | 41±1.8 g | 120±6.2 |
| (Maquoi et al., 2003) | Mouse | B10.RIII | Male | 7 to 11 | 20 wk. | HFD | 15 wk. | 37±1.5 g | Gonadal fat | Computer-assisted image analysis | 210±17 |
| (Lijnen et al., 2007) | Mouse | C57Bl/6 | Male | 8 | 20 wk. | HFD | 15 wk. | 42±1.4 g | Gonadal fat | Computer-assisted image analysis | 238±16 |
| (Van Hul et al., 2012) | Mouse | C57Bl6/129SvJ/EMS + Ter | Male | 10 to 14 | 20 wk. | SFD | 15 wk. | 23±0.46 g | Gonadal fat | Computer-assisted image analysis | 740±96 |
| 10 to 14 | HFD | 27±0.72 g | 400±55 |

* **Capillary wall thickness**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Sex** | **Age** | **Diet** | **Duration of diet** | **Body weight** | **Location** | | **Method** | **Value** |
| (Simionescu et al., 1978) | Mouse | Male | ? | SFD | 7 or 10 days | 20-30 g | Bipolar microvascular fields in diaphragm | Middle segment of capillaries | Measure attenuated part of endothelial cell | 0.25±0.05 µm |
| Venular segment of capillaries | 0.17±0.07 µm |
| (Ahrendt et al., 2020) | Mouse | Male | 35 wk. | SFD | 30 wk. | 30-45 g | Lung | | Endothelial cell thickness (Stereology; photo + line grids + # of points) | 0.18 µm (approx.) |
| HFD | 50-55 g | 0.28 µm (approx.) |
| (Van den Berg et al., 2003) | Rat | Male | ? | - | - | 250-350 g | Myocardial capillaries | | = (Outer capillary diameter) – (inner capillary diameter) | 0.18±0.04 µm |
| (Lash et al., 1989) | Zucker rat | Male | 11 wk. | Lean | 6 wk. (ad libtum) | ? | Plantar muscle | | Endothelial thickness  (photo) | 0.174±0.004 µm |
| Genetic obesity | 6 wk. (ad libtum) | 0.203±0.007 µm |
| 18 wk. | Lean | 13 wk. (ad libtum) | 0.147±0.005 µm |
| Genetic obesity | 13 wk. (ad libtum) | 0.136±0.004 µm |
| (Cinti, 2018) | Rat |  | ?  (young) | ? | ? | ? | Epididymal adipose tissue | | Attenuated part of endothelial cell (measured by YLee) | >0.2 µm (approx.) |

* **Capillary basement membrane (CBM) thickness**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Age** | **n** | **Status** | **Body weight** | **Location** | | | | **Method** | **Value** |
| (Cuthbertson & Mandel, 1986) | CBA Mouse  (male) | 1.5 mo. | 4 | Normal | ? | Retina  (mid-zone) | | | | Transmission electron microscopy (TEM) (thickness) = (CBM area)  /(circumference) | 50±9 nm |
| 4 mo. | 4 | 59±13 nm |
| 8 mo. | 4 | 75±10 nm |
| 12 mo. | 4 | 108±17 nm |
| 20 mo. | 4 | 154±27 nm |
| Balb/c  (female) | 1.5 mo. | 2 | 55±9 nm |
| 8 mo. | 2 | 77±9 nm |
| 20 mo. | 2 | 158±35 nm |
| 1.5 mo. | 2 | Retina (center) | | | | 41±4 nm |
| 1.5 mo. | 2 | Retina (periphery) | | | | 64±6 nm |
| (Rodrigues et al., 1983) | SJL/J  Mouse  (Male) | 5-6 wk.+  6 mo.  (7 mo.) | ? | Normal  (Uninfected) | ? | Retina | | | | Transmission electron microscopy (TEM) | 69±5.5 nm |
| 8 | Diabetes  (EMC virus infected) | 91±10.2 nm |
| 12 | Normal  (Uninfected) | Kidney | | | | 91±3 nm |
| 12 | Diabetes  (EMC virus infected) | 382±6 nm |
| (Ceafalan et al., 2019) | C57BL/6J  Mouse | 6 mo. | 100 | Normal | ? | Brain | | | | Transmission electron microscopy (TEM) | 56.78±12.50 nm |
| 24 mo. | 100 | Normal | ? | 107.53±23.76 nm |
| (Creutzfeldt et al., 1970) | Spiny mouse | 220±146 days  (7±5 mo.) | 8 | Normal | 45±10 g | Gastrocnemius (muscle) | | | | Electron microscopy | 73±16 nm |
| 254±190 days  (8.5±6.3 mo.) | 6 | Moderately impaired glucose tolerance | 49±7 g | 75±18 nm |
| 207±125 days  (7±4 mo.) | 6 | Severely impaired glucose tolerance | 50±11 g | 80±18 nm |
| 462±174 days  (15.4±6 mo.) | 5 | Spontaneous severe diabetes | ? | 105±9 nm |
| (Carlson et al., 2003) | Control vs. OVE26  Mouse | 300-350 days  (10 – 12 mo.) | 8 | Normal | 39.40±3.11 g | Retina | | | | Transmission electron microscopy (TEM) morphometry  (Intersection of CBM with sampling grid lines) | 92.87±18.90 nm |
| 14 | Genetic diabetes | 40.52±3.16 g | 113.09±9.57 nm |
| 10 | Normal | 39.40±3.11 g | Extensor digitorum  (muscle) | | | | 76.75±14.17 nm |
| 8 | Genetic diabetes | 40.52±3.16 g | 72.10±16.85 nm |
| 19 | Normal | 39.40±3.11 g | Kidney | | | | 178.16±35.61 nm |
| 12 | Genetic diabetes | 40.52±3.16 g | 333.19±66.07 nm |
| 8 | Normal | 39.40±3.11 g | Pulmonary alveolus | | | | 67.99±6.95 nm |
| 8 | Genetic diabetes | 40.52±3.16 g | 77.02±8.97 nm |
| 8 | Normal | 39.40±3.11 g | Diaphragm  (muscle) | | | | 54.75±5.00 nm |
| 8 | Genetic diabetes | 40.52±3.16 g | 67.98±2.81 nm |
| 8 | Normal | 39.40±3.11 g | Pancreas | | | | 103.54±16.33 nm |
| 6 | Genetic diabetes | 40.52±3.16 g | 120.77±28.05 nm |
| 3 | Normal | 39.40±3.11 g | Choroid | | | | 78.58±7.06 nm |
| 5 | Genetic diabetes | 40.52±3.16 g | 81.73±12.71 nm |
| 12 | Normal | 39.40±3.11 g | Heart IVS\* | | | | 63.13±5.91 nm |
| 13 | Genetic diabetes | 40.52±3.16 g | 69.85±12.34 nm |
| 12 | Normal | 39.40±3.11 g | Heart LV\*\* | | | | 56.92±4.02 nm |
| 12 | Genetic diabetes | 40.52±3.16 g | 62.97±9.64 nm |
| 15 | Normal | 39.40±3.11 g | Peripheral nerve | | | | 58.75±9.86 nm |
| 5 | Genetic diabetes | 40.52±3.16 g | 58.64±4.55 nm |
| (Williams et al., 2020) | Male  C57Bl/6 mice | 22 wk.  (5.5 mo.) | 31 | Lean | 28.676 g | Skeletal muscle  (gastrocnemius) | | | | Electron microscopy | 107.62±5.482 nm  (Mean±SE) |
| 31 | Obese | 43.588 g | 102.7±6.44 nm  (Mean±SE) |
| (Chang et al., 2012) | FVB/NJ vs. Akita FVB/NJ  Mouse | 30 wk.  (7.5 mo.) | 4 | Normal | ? | Kidney | | | | Transmission electron microscopy (TEM) | 224.2±27.7 nm  (Mean±SE) |
| 4 | Genetic diabetes  (Akita) | ? | 240.8±77.5 nm  (Mean±SE) |
| (Velic et al., 2013) | FVB | 350 days  (11.7 mo.) | 7 | Normal | 23.90±0.52 g | Heart LV | | | | Transmission electron microscopy (TEM) | 48.50±7.31 nm |
| Mt (over-express MT) | 4 | Normal & overexpressing MT | 25.60±1.82 g | 44.56±3.62 nm |
| OVE | 8 | Genetic diabetes | 23.60±0.95 g | 62.18±10.34 nm |
| OVEMt (OVE+Mt) | 7 | Genetic diabetes & overexpressing MT | 23.30±1.14 g | 47.28±7.07 nm |
| (Kuiper et al., 2008) | BALBc/129Sv crossed with C57Bl/6J | 33 wk.?  (16 wk. +17 wk.) | ? | Normal | ? | Retina | | jBL | | **Electron microscopy**  Method 1: inner basal lamina (jBL) vs. outer basal lamina (eBL+pBL) | 0.12 µm |
| ? | eBL+pBL | | 0.148 µm |
| ? | eBL | | **Electron microscopy**  Method 2: BL of the endothelial cell (eBL), BL of the pericyte (pBL), and joint BL of both endothelial cell and peri- cyte (jBL) | 0.142 µm |
| ? | pBL | | 0.165 µm |
| ? | jBL | | 0.115 µm |
| (Hawkes et al., 2013) | Male and female C57BL/6 | 2 mo. | 3 | Normal | ? | Brain (Striatum) | | | | Electron microscopy | 67.03±4.34 nm  (mean±SE) |
| 3 | Brain (Cortex) | | | | 65.79±5.56 nm  (mean±SE) |
| 3 | Brain (Hippocampus) | | | | 62.58±2.70 nm  (mean±SE) |
| 3 | Brain (Thalamus) | | | | 70.11±3.63 nm  (mean±SE) |
| 7 mo. | 3 | Brain (Striatum) | | | | 74.94±6.62 nm  (mean±SE) |
| 3 | Brain (Cortex) | | | | 57.35±4.33 nm  (mean±SE) |
| 3 | Brain (Hippocampus) | | | | 63.50±4.78 nm  (mean±SE) |
| 3 | Brain (Thalamus) | | | | 58.62±5.17 nm  (mean±SE) |
| 23 mo. | 3 | Brain (Striatum) | | | | 74.23±2.80 nm  (mean±SE) |
| 3 | Brain (Cortex) | | | | 97.49±12.27 nm  (mean±SE) |
| 3 | Brain (Hippocampus) | | | | 109.50±11.93 nm  (mean±SE) |
| 3 | Brain (Thalamus) | | | | 108.43±14.51 nm  (mean±SE) |
| (Mehta et al., 2013) | Mouse | 18–20 mo. | 3 | Normal | ? | Brain  (primary motor cortex and parieto-temporal cortex) | | | | **Fluorescence microscope**  The apparent thickness of the vascular basement membrane was assessed immunohistochemically by measuring collagen-IV deposition in WT and 3×TG mice | 500±27 nm  (mean±SE) |
| 3 | Alzheimer’s disease | ? | 754±25 nm  (mean±SE) |
| (Lash et al., 1989) | Zucker rat | 11 wk.  (2.75 mo.) | 6 | Lean (FA/fa) | ? | Plantar muscle | | | | Electron microscopy  (thickness) = (CBM area)  /(circumference) | 61.87±1.33 nm  (Mean±SE) |
| 6 | Genetic obesity (fa/fa) | 68.13±1.66 nm  (Mean±SE) |
| 6 | Genetic obesity + exercise (6-11 wk.) | 65.10±1.43 nm  (Mean±SE) |
| 18 wk.  (4.5 mo.) | 6 | Lean (Fa/fa) | 55.67±1.04 nm  (Mean±SE) |
| 7 | Genetic obesity (fa/fa) | 57.82±1.24 nm  (Mean±SE) |
| 6 | Genetic obesity + exercise  (11-18 wk.) | 63.70±1.29 nm  (Mean±SE) |
| 6 | Genetic obesity + exercise  (6-18 wk.) | 65.57±1.48 nm  (Mean±SE) |
| (A. Dosso et al., 1990) | Male Zucker rat | 68 wk.  (17 mo.) | 5 | Lean (FA/FA) + standard chow | ? | Retina | | | | Electron microscopy | 93.6±6.12 nm |
| 4 | Obese (fa/fa) + standard chow | 104.6±4.58 nm |
| 6 | Lean (FA/FA) + Sucrose | 97.4±2.82 nm |
| 3 | Obese (fa/fa) + Sucrose | 99.6±9.78 nm |
| (Fraselle-Jacobs et al., 1987) | Male albino Wistar rats | 6 mo. | 1 | Normal | 334.5±16.8 g | Epididymal adipose tissue | Basement membrane | | | Electron microscope morphometry + Image J by Yunjeong | [108.78±11.2 nm](geometric/capillary%20basement%20membrane/Fraselle_Jacobs_measurements.csv)  (Mean±SE)  ([98.28−145.17 nm](geometric/capillary%20basement%20membrane/Screen%20Shot%202022-12-15%20at%2011.31.59%20AM.tif)) |
| 5 | Lamina lucida | | | Electron microscope morphometry | 21.7±2.5 nm |
| Basal lamina  (Lamina densa) | | | 43.1±3.0 nm |
| 24 mo. | 5 | 358.5±14.7 g | Epididymal adipose tissue | Lamina lucida | | | Electron microscope morphometry | 21.9±2.1 nm |
| Basal lamina  (Lamina densa) | | | 26.9±2.6 nm |
| (Danis & Yang, 1993) | Male Zucker rat | 6-7 mo. | 4 | Lean (Fa/fa) | ? | Retina | | | | Transmission electron microscopy (TEM) | 89.0±1.958 nm |
| 4 | Genetic obesity & diabetes (fa/fa) | 113.4±1.78 nm |
| (Cherian et al., 2009) | Sprague-Dawley rat | > 6 mo. | 6 | Normal | ? | Retina | | | | Electron microscopy | 50.8±5.1 nm |
| Kidney | | | | 81±9.9 nm |
| 6 | Diabetes | Retina | | | | 69.2±15.9 nm |
| Kidney | | | | 111.4±25.2 nm |
| 6 | Tightly controlled diabetes | Retina | | | | 53.6±3.3 nm |
| Kidney | | | | 86.7±6.3 nm |
| (Gambaro et al., 1992) | Male Sprague-Dawley rats | 8 mo. + 6-7 wk.  (9-10 mo.) | 3 | Normal | 694.5±17.2 g | Kidney | | | | Electron microscopy | 235.57±1.05 nm  (mean±SE) |
| 3 | STZ-induced diabetes | 380.2±11.9 g | 346.19±1.11 nm (mean±SE) |
| 3 | STZ-induced diabetes+low molecular weight heparin | 378.8±12.7 g | 221.85±1.08 nm (mean±SE) |
| 3 | STZ-induced diabetes+ Dermatan sulphate | 363.4±18.5 g | 260.08±1.06 nm  (mean±SE) |
| (Yagihashi, 1978) | Wistar rats | 4 wk.  (1 mo.) | 4 | Normal | 109±14 g | Kidney | | | | Electron microscopy | 119.0±6.8 nm |
| 8 wk.  (2 mo.) | 4 | Normal | 224±17 g | 129.1±4.6 nm |
| 12 wk.  (3 mo.) | 4 | Normal | 278±13 g | 135.4±3.5 nm |
| 16 wk.  (4 mo.) | 4 | Normal | 313±10 g | 147.3±1.3 nm |
| 20 wk.  (5 mo.) | 4 | Normal | 345±18 g | 154.1±3.5 nm |
| 24 wk.  (6 mo.) | 4 | Normal | 404±48 g | 160.5±3.8 nm  (mean±SD) |
| 28 wk.  (7 mo.) | 4 | Normal | 488±41 g | 184.6±6.5 nm  (mean±SD) |
| 32 wk.  (8 mo.) | 4 | Normal | 563±48 g | 205.3±7.2 nm |
| 36 wk.  (9 mo.) | 4 | Normal | 624±40 g | 238.3±11.4 nm |
| (Fox et al., 1977) | Male  Wistar rats | > 14 mo.+11 wk.  (total 17 mo.) | 6 | STZ-induced diabetes+normal diet | 436±14 g | Kidney | | | | Electron microscopy | 431±18 nm |
| 6 | STZ-induced diabetes+low carbohydrate diet | 444±29 g | 389±15 nm |
| 6 | STZ-induced diabetes+ insulin +normal diet | 459±10 g | 414+8 nm |
| 5 | STZ-induced diabetes+insulin + low carbohydrate diet | 604±50 g | 400±26 nm |
| 6 | Normal+normal diet | 598±24 g | 305±10 nm  (mean±SE) |
| 6 | Normal+low carbohydrate diet | 655±35 g | 349±22 nm  (mean±SE) |
| (Saito et al., 2003) | Male OLEFT rats  vs.  LEFT rats | 22 wk.  (5.5 mo.) | 50 (5 rats) | Normal | 506±22 g | Heart | | | | Electron microscopy | 90±12 nm |
| 62 wk.  (15.5 mo.) | 50 (5 rats) | 528±18 g | 87±12 nm |
| 22 wk.  (5.5 mo.) | 50 (5 rats) | Obese with diabetes | 644±32 g | 106±20 nm |
| 62 wk.  (15.5 mo.) | 50 (5 rats) | 523±90 g | 177±66 nm |
| (Begieneman et al., 2009) | Rats | ? | 6 | Normal | ? | Heart  (left ventricular) | | | | Electron microscopy | 68.736±4.22 nm  (mean±SE) |
| ? | 5 | acute myocardial infarction | ? | 76±9.85 nm  (mean±SE) |
| (Osawa et al., 2003) | Wistar rat | 3 mo. | 3? | Normal | ? | Facial nerve | | | Lamina lucida | Transmission electron microscopy (TEM) | 41.440±1.156 nm (mean±??) |
| Lamina densa | 43.420±1.196 nm  (mean±??) |
| (Das et al., 1990) | Female Wistar-Kyoto albino rat | 10.5 mo  (6 wk. age + 9 mo. diet) | 5 | Normal | ? | Retina | | | Inner nuclear layer | **Image analysis**   * BMA: basement membrane area * BMP: basement membrane perimeter, taken by summing both inner and outer perimeters * BML: basement membrane length * BMT: basement membrane thickness   BML = BMP/2  BMT = BMA/BML | 166.7±44.5 nm  (mean±SD) |
| 5 | ? | Nerve fiber layer | 206.5±42.3 nm  (mean±SD) |
| 5 | Galactose fed | ? | Inner nuclear layer | 280.6±69.7 nm  (mean±SD) |
| 5 | ? | Nerve fiber layer | 316.4±80.3 nm (mean±SD) |
| 5 | Galactose+Sorbinil fed | ? | Inner nuclear layer | 164.0±31.2 nm (mean±SD) |
| 5 | ? | Nerve fiber layer | 214.6±50.2 nm  (mean±SD) |
| (Robison et al., 1983) | Male Sprague-Dawley rat | >28 wk.  (>7 mo.) | 3 | Control | ? | Retina  (outer plexiform layer) | | | | **Electron microscopy**   * BMA: basement membrane area * BML: basement membrane length * T: the total cross-sectional area of each capillary * M: mural (pericyte) cell area * E: endothelial cell area(E) * Lu: lumen area   BMA = T-(M+E+Lu)  BML = [length of lines delimiting BMA]/2  BMT = BMA/BML | 96.7±14.1 nm  (mean±SD) |
| 3 | Galactose fed | ? | 151.9±18.7 nm (mean±SD) |
| 3 | Galactose+Sorbinil fed | ? | 99.1±14.1 nm  (mean±SD) |
| >44 wk.  (>11 mo.) | 4 | Control | ? | 93.9±12.3 nm (mean±SD) |
| 4 | Galactose fed | ? | 194.4±40.4 nm  (mean±SD) |
| 4 | Galactose+Sorbinil fed | ? | 105.8±17.2 nm  (mean±SD) |
| (Roy et al., 2003) | Male Sprague-Dawley rat | >7 mo. | 5 | Control | ~200 g  (beginning of the experiment) | Retina  (outer plexiform layer) | | | | Electron microscopy | 85±20 nm  (mean±SD) |
| 5 | Galactose fed | 139±16 nm  (mean±SD) |
| 5 | Galactose fed+antisense oligos | 105±24 nm  (mean±SD) |
| (Evans et al., 2000) | Male Sprague-Dawley rat | >6 mo. | 8 | Control | 631.8±23.51 g | Retina  (outer plexiform and inner nuclear layer) | | | | Electron microscopy | 66.142±2.756 nm  (mean±SE) |
| 8 | Diabetes | 495.2±15.2 g | 113.268±5.236 nm  (mean±SE) |
| 8 | Diabetes with Bosentan† | 484.9±9.8  g | 84.606±3.307 nm  (mean±SE) |
| 8 | Galactose-fed | 542.2±17.2 g | 119.331±4.685 nm  (mean±SE) |
| 8 | Galactose with Bosentan | 529.2±9.2 g | 84.055±4.409 nm  (mean±SE) |
| (Zheng et al., 2007) | Male Sprague-Dawley rat | >32 wk.  (>8 mo.) | 8 | Control | 250~300 g | Retina  (outer plexiform layer) | | | | Transmission electron microscopy (TEM) | 75.658±10.526 nm  (mean±SD) |
| 8 | Control treated with propranolol | 73.355±7.895 nm  (mean±SD) |
| 8 | Control treated with fosenopril sodium | 73.684±9.868 nm  (mean±SD) |
| 8 | Diabetes | 171.053±19.408 nm  (mean±SD) |
| 8 | Diabetes treated with propranolol | 164.474±15.789 nm  (mean±SD) |
| 8 | Diabetes treated with fosenopril sodium | 93.421±11.184 nm  (mean±SD) |
| (Gardiner et al., 2003) | Male Wistar albino rat | >12 mo. | 6 | Diabetic | ~250 g | Retina  (Central region) | | | | Electron microscopy  +  Stereological analysis | * Volume: 9.09±0.53 µm3 * Surface area/unit volume: 36.03±3.27/µm * Thickness: |
| 6 | Diabetic+ aminoguanidine | * Volume: 5.9±0.48 µm3 * Surface area/unit volume: 28.44±2.74/µm * Thickness: |
| 6 | Control | * Volume: 5.78±0.37 µm3 * Surface area/unit volume: 26.92±2.34/µm * Thickness: |
| 6 | Control+ aminoguanidine | * Volume: 5.74±0.17 µm3 * Surface area/unit volume: 27.97±2.74/µm * Thickness: |
| (A. A. Dosso et al., 2004) | Male Wistar Kyoto rat | 27 wk.  (<7 mo.) | 7 | Control  (normotensive non-diabetic) | 429±21 g | Retina  (outer plexiform layer) | | | | Electron microscopy | 111.8±14.2 nm  (mean±SD) |
| 7 | normotensive diabetes | 165±11 g | 132.8±19.4 nm  (mean±SD) |
| 7 | normotensive diabetes +cilazapril | 160±22 g | 131.9±17.3 nm  (mean±SD) |
| Male spontaneously hypertensive rat | 7 | hypertensive diabetic | 175±15 g | 150.3±20.2 nm  (mean±SD) |
| 7 | hypertensive diabetes +cilazapril | 190±28 g | 116.7±11.0 nm  (mean±SD) |
| (Frank et al., 1983) | Female Normotensive Wistar Kyoto | 6 mo. | 4 | Control | ? | Retina  (inner nuclear and inner plexiform layers) | | | | Light microscopy | 81.58±7.89 nm  (mean±SE) |
| 9 mo. | 4 | ? | 94.74±7.89 nm  (mean±SE) |
| 12 mo. | 4 | ? | 121.05±19.3 nm  (mean+SE) |
| 6 wk.+ 15–21 mo.  (16.5–22.5 mo.) | 7 | 331±4 g | 160.4 ± 31.2 nm  (mean±SD) |
| 7 | 30% galactose-fed | 285 ± 28 g | 203.3 ± 37.6 nm  (mean±SD) |
| 9 | 30% galactose-fed+Sorbinil | 282 ± 11 g | 159.4 ± 35.2 nm  (mean±SD) |
| Female spontaneously hypertensive rat | 6 wk.+ 15–21 mo.  (16.5–22.5 mo.) | 7 | Control | 30-40 g lighter than WKY rats | 159.4 ± 36.1 nm  (mean±SD) |
| 6 | 30% galactose-fed | 230.7 ± 62.3 nm  (mean±SD) |
| 8 | 30% galactose-fed+Sorbinil | 154.3 ± 43.5 nm  (mean±SD) |
| (Chakrabarti & Sima, 1989) | Male prediabetic diabetes-prone BB rat | >3 wk.+6 mo.  (> 7 mo.) | 5 | Diabetes | 306 g | Retina | Superficial | | | Electron microscopy | 192.2 ± 5.8 nm  (mean±SE) |
| 5 | Deep | | | 139.9 ± 5.8 nm  (mean±SE) |
| 5 | Diabetes+ ponalrestat | 275 g | Superficial | | | 175.7 ± 4.5 nm  (mean±SE) |
| 5 | Deep | | | 99.9 ± 9.2 nm  (mean±SE) |
| 5 | Diabetes+insulin | 366 g | Superficial | | | 134.0 ± 6.9 nm  (mean±SE) |
| 5 | Deep | | | 97.7 ± 7.0 nm  (mean±SE) |
| Male non-diabetes- prone male BB rat | 5 | Control | 495 g | Superficial | | | 134.6 ± 7.7 nm  (mean±SE) |
| 5 | Deep | | | 95.1 ± 3.3 nm  (mean±SE) |
| 5 | Control+ ponalrestat | 456 g | Superficial | | | 127.9 ± 6.9 nm  (mean±SE) |
| 5 | Deep | | | 82.8 ± 8.5 nm  (mean±SE) |
| (McCaleb et al., 1991) | Female Wistar rat | >10 wk.+8 mo.  (>10.5 mo.) | 6 | Control | 324±7 g | Retina  (outer plexiform layer) | | | | Electron microscopy | 84.403±1.162 nm  (mean±SE) |
| 12 | Diabetes | ? | 124.281±5.42 nm  (mean±SE) |
| 12 | Diabetes+tolrestat | ? | 98.341±4.646 nm  (mean±SE) |
| (Smith et al., 1995) | Male Sprague-Dawley rat | >6 mo. | ? | Control | Approx. 550 g | Inner ear | | | | Electron microscopy | 102±9 nm  (mean±SE) |
| ? | Diabetes | Approx. 350 g | 177±10 nm (mean±SE) |
| ? | Noise-exposed control | Approx. 470 g | 97±1 nm  (mean±SE) |
| ? | Noise-exposed diabetes | Approx. 330 g | 175±5 nm (mean±SE) |
| (Robison et al., 1986) | Male CRL:COBS-CD (SD) Sprague-Dawley rat | >7 mo. | 4 | Control | ? | Retina  (outer plexiform layer) | | | | Electron microscopy | 122.9±19.6 nm  (mean±SD) |
| 4 | 50% galactose-fed | ? | 200.1±39.9 nm  (mean±SD) |
| 4 | 50% galactose-fed + 0.03% tolrestat | ? | 130.1±19.6 nm  (mean±SD) |
| 4 | 50% galactose-fed + 0.04% tolrestat | ? | 120.3±15.7 nm  (mean±SD) |
| (Clements et al., 1998) | Male db/m | 22 wk.  (5.5 mo.) | ? | Normal | ? | Retina  (outer plexiform layer) | | | | Electron microscopy | 79.4±1.9 nm  (mean±SE) |
| Male db/db | ? | Diabetes | ? | 87.3±3.4 nm  (mean±SE) |
| ? | Diabetes+A717 | ? | 83.8±1.8 nm  (mean±SE) |
| (Sima et al., 1988) | Male Lewis rats of the AC1 (AgB4/4) strain | >4 mo. | 5 | Control | 329±29 g | Retina  Superficial capillary bed | | | | **Electron microscopy**   * BMA: basement membrane area * BML: basement membrane length * T: the total cross-sectional area of each capillary * P: pericyte cell area * E: endothelial cell area(E) * L: lumen area   BMA = T-(P+E+L)  BML = [length of lines delimiting BMA]/2  BMT = BMA/BML | 146.2±6.7 nm  (mean±SD) |
| Retina  Deep capillary bed | | | | 97.4±7.5 nm  (mean±SD) |
| (Kern & Engerman, 1994) | Male Sprague-Dawley rat | >20 mo. | 13 | Control | ? | Retina  (outer plexiform layer or inner nuclear layer) | | | | Electron microscopy | 159±23 nm  (mean±SD) |
| 18 | Diabetes | ? | 216±36 nm  (mean±SD) |
| 6 | 30% galactose | ? | 227±37 nm  (mean±SD) |
| 6 | 50% galactose | ? | 276±26 nm  (mean±SD) |
| (Chakrabarti et al., 1991) | BB-rat | >6 mo. | ? | Control | 539.0±21.6 g | Superficial retinal capillary | | | | **Electron microscopy**  BMA = T-(P+E+L)  BML = [length of lines delimiting BMA]/2  BMT = BMA/BML | 161.9±3.7 nm  (mean±SE) |
| Deep retinal capillary | | | | 142.7±3.3 nm  (mean±SE) |
| Muscle | | | | 125.0±3.2 nm  (mean±SE) |
| Endoneurial capillary | | | | 142.8±4.5 nm  (mean±SE) |
| Kidney | | | | 326.0±20.0 nm  (mean±SE) |
| (Roy et al., 2011) | Male Sprague Dawley rat | >6 mo. | 8 | Control | ? | Retina  (outer plexiform layer) | | | | Electron microscopy | 51.5±4.8 nm  (mean±SD) |
| 8 | Diabetes | ? | 72.5±5.0 nm  (mean±SD) |
| 8 | Diabetes+ FN-siRNA‡ | ? | 56.4±2.8 nm  (mean±SD) |
| 8 | Diabetes+ scrambled siRNA | ? | 73.7±3.9 nm  (mean±SD) |
| (Li et al., 2018) | male Sprague-Dawley rat | 33 wk.  (8 mo.) | 6 | Control | 577.4 ± 36.1 g | Retina  (outer plexiform and ganglion cell layers) | | | | Transmission electron microscopy (TEM) | 94.6±7.7 nm  (mean±SD) |
| 6 | Diabetic | 343.5 ± 31.3 g | 212.4±18.1 nm  (mean±SD) |
| 6 | Diabetic+ Fenofibrate | 381.2 ± 28.7 g | 129.3±9.4 nm  (mean±SD) |
| (Belligoli et al., 2019) | Human | 48±12 y | 6 | Lean | ? | Visceral adipose tissue | | | | Transmission electron microscopy (TEM) | 103.38 nm  [67.23, 194.26]  (Median, 95% percentile) |
| 41±9 y | 5 | Obese without diabetes | 108.78 nm  [60.47, 181.76]  (Median, 95% percentile) |
| 45±10 y | 5 | Obese with prediabetes | 116.56 nm  [68.79, 208.28]  (Median, 95% percentile) |
| 52±9 y | 5 | Obese with type 2 diabetes | 139.87 nm  [68.24, 209.12]  (Median, 95% percentile) |

\* Heart IVS: interventricular septal sample

\*\* Heart LV: left ventricular sample

† Bosentan: Endothelin receptor blocker

‡ FN-siRNA: siRNA approach targeting fibronectin

* **~~Adipocyte~~ basement membrane (ABM) thickness**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Age** | **Status** | **Body weight** | **Location** | **Method** | **Value** |
| (Fraselle-Jacobs et al., 1987) | Rat | 6 mo. | Normal | 250-500 g  (Mean: 350g) | Epididymal adipose tissue | Electron microscope morphometry | nm |
| (Comley & Fleck, 2010) | Porcine | ? | ? | ? | Dermis adipose tissue | Scanning electron microscope & laser confocal microscope  (Reinforced basement membrane) |  |
| (Abrahamson, 1986) | ? | ? | ? | ? | ? | ? | 100 nm |
| (Marilyn G. Farquhar, 1978) | ? | ? | ? | ? | ? | ? | 20 – 50 nm |
| (Farquhar & Palade, 1965) | Toad | Adult | ? | ? | Skin epidermis | Light microscopy | < 30 nm |
| < 50 nm |

**A picture containing mirror, hand glass, bowed instrument

Description automatically generated**

Basement membrane

= lamina lucida

+ lamina densa (basal lamina)

+ reticular lamina

**(Fraselle-Jacobs *et al*., 1987)**

* **Pore size in basement membrane (diameter)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Age** | **Status** | **Body weight** | **Location** | **Method** | **Value** |
| (Antonio Martinez-Hernandez, 1978) | Mouse | ? | ? | ? | Kidney  (Glomerular BM) | Routine electronic microscopy |  |
| Parietal  yolk sac carcinoma  (Neoplastic basement membrane) |
| (Sarin, 2010) | ? | ? | ? | ? | Capillary in adipose tissue | ? | < 5 nm |
| (Carpita et al., 1979) | Plants | ? | ? | ? | Hair cells/palisade parenchyma cells  (Cell wall; Semi-dehydrated ECM) | Phase-contrast microscopy | 7 – 10.4 nm |

* **Pore size in extracellular matrix in adipose tissue (diameter)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Age** | **Status** | **Body weight** | **Location** | **Method** | **Value** |
| (Song et al., 2018) | Human | 20-40 yr | Healthy | ? | Decellularized human adipose tissue-derived ECM scaffolds extracted from abdomen | Scanning electron microscopy | 20–200µm |

* **Endothelial cell area**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Age** | **Diet** | **Body weight** | **Location** | **Method** | **Value** |
| (Haas & Duling, 1997) | Golden hamster | ? | ? | ? | Cheek pouch **arterioles** | Bright-field video microscopy | 945.2−1029.6 |
| (Behndig et al., 2001) | Mouse | 4 mo. | ? | ? | Central corneal endothelium | Light microscopy | 365.36  [320, 425.71] |
| (Behndig, 2008) | Mouse | 10.4±3.0 mo. | ? | ? | Central corneal endothelium | Light microscopy | 246±35 |
| (Ahrendt et al., 2020) | Mouse | 35 wk. | SFD | 30-45 g | Lung | Surface area of endothelial cells facing the capillary lumen  (Stereology; photo + line grids + # of points) | 150−250 (approx.) |
| HFD | 50-55 g | 150−290 (approx.) |

\* [,] shows minimum and maximum value.

* **Endothelial cell volume**

|  |  |  |  |
| --- | --- | --- | --- |
| **Reference** | **Cell** | **Method** | **Value** |
| (Baydoun et al., 1990) | Bovine aortic endothelial cell | 1. Bovine aortic endothelial cells (EC) were isolated using 0.5 mg/ml collagenase (Boehringer) and grown to confluence in 25 cm2 flasks. 2. EC volume was also measured using the ELZONE apparatus calibrated with standard Latex beads (Sigma). | 1.02 pL |

* **Interstitial/extracellular fluid volume fraction**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Sex** | **Age** | **Diet** | **Body weight** | **Location** | **Method** | **Inter/extra** | **Value** |
| (Eigenmann et al., 2017) | Mouse | Both | 8-12 wk. | ad libitum | 19-34 g (mean: 23 g) | Adipose | 1. Get extracellular volume fraction using 51Cr-EDTA injection 2. Get residual plasma space by 125I-HAS injection 3. Get interstitial volume fraction by: (Int. vol. frac.) = (Ext. vol. frac.) – (Res. pl. vol. frac.) | Extracellular | 0.101  in ml/g tissue |
| Interstitial | 0.093  in ml/g tissue |
| (Digirolamo & Owens, 1976) | Wistar rat | Male | 1.2-16 mo. | ad libitum | 110-750 g | Epididymal fat | 1. Extract lipid and determine triglyceride and defatted dry residue (DDR). (tissue water) = (tissue wet weight) – (weight of lipid) – (DDR) 2. ??? (intracellular water) = (tissue water) – (extracellular water) | Outside of adipocytes | 0.160 in ml/g tissue |

* **VEGF165:VEGFR1 binding affinity**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | | **Ligand/receptor source** | **()** | **()** |  |
| (Yen et al., 2011) |  |  |  | |  |  |  | 33 pM |
| (Waltenberger et al., 1994) | Recombinant 125I-VEGF165 expressed in baculovirus system | Human VEGFR1 on PAE cells or HUVECs | Radioligand  (Competitive binding) | | Porcine aortic endothelial **(PAE) cells** transfected with a VEGFR1-expressing vector | ? | ? | 16 pM |
| **HUVECs** | 9 pM |
| (Mamer et al., 2020) | Recombinant VEGF165  **(10, 20, 40nM)** | Immobilized recombinant VEGFR1 protein | SPR | | Obtained from R&D Systems |  |  | pM |
| (Teran & Nugent, 2019) | Recombinant VEGF165 | Immobilized VEGFR1 Fc\* chimera | SPR | | Obtained from R&D Systems |  |  | pM |
| (Von Tiedemann & Bilitewski, 2002) | VEGF165 | Immobilized sVEGFR1 | SPR | | **VEGF165 & VEGFR1**  Sf158 insect cells infected with a baculovirus-based vector (both ligand and receptor) |  |  | pM |
| sVEGFR1 on microtiter plates | Radioligand (Saturation analysis; Scatchard analysis) | | ? | ? | 74±7.4 pM |
| (Papadopoulos et al., 2012) | VEGF165 | Human  VEGFR1-hFc§ | SPR | | **VEGF165**  Made at Regeneron Pharmaceuticals  **Human VEGFR1-hFc**  Obtained from R&D systems |  |  | pM |
| (Jin et al., 2007) | 125I-VEGF165 | VEGFR1 on adventitial fibroblasts | Radioligand  (Saturation analysis) | | **VEGF165**  Obtained from R&D Systems  **VEGFR1**  adventitial fibroblasts from thoracic aorta of 6–8-week-old male Sprague–Dawley (SD) rats | ? | ? | pM |
| (Breier et al., 1995) | Recombinant 125I-VEGF165 | VEGFR1 on COS cells | Radioligand  (Saturation  analysis) | Non-linear regression curve | **VEGF165**  Expressed in Sf9 insect cells  **VEGFR1**  COS cells transfected with murine full length VEGFR1 cDNA | ? | ? | 90 pM |
| Scatchard analysis | 114 pM |
| (Ito & Claesson-Welsh, 1999) | VEGF165 | VEGFR1 on PAE cells | Radioligand  (Saturation analysis; Scatchard) | No heparin | **VEGF165**  From PeproTech. Inc  **VEGFR1**  PAE cells transfected with human VEGFR1 cDNA | ? | ? | 54 pM |
| Heparin 0.5 µg/ml | 77 pM |
| Heparin  5 µg/ml | 118 pM |
| (Rouet et al., 2005) | Recombinant 125I-VEGF165 | VEGFR1-Fc chimera† | ELISA plate+Saturation analysis  (Scatchard) | | **VEGF165**  expressed in Sf9 insect cells  **VEGFR1**  R&D Systems | ? | ? | 59.4±19.6 pM |

\* Fc: pre-dimerized

§ The extracellular domains of dimerized human VEGFR1 or VEGFR2 fused inline to hFc

† The extracellular domain of VEGFR1

* **VEGF165:VEGFR2 binding affinity**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | **Ligand/receptor source** | **()** | **()** |  |
| (Yen et al., 2011) |  |  |  |  |  |  | 100 pM |
| (Huang et al., 1998) | Recombinant VEGF165  (**50 nM**) | Recombinant sVEGFR2  (Full length **mouse** Flk-1 cDNA) | SPR | **VEGF165**  R&D Systems  **VEGFR2**  Spodoptera frugiperda (Sf9) infected with sVEGFR2 recombinant baculovirus |  |  | 340 pM |
| Recombinant VEGF165  (**5 nM**) |  |  | 110 pM |
| Recombinant **VEGF164**  (**20 nM**) |  |  | 330 pM |
| Recombinant **VEGF164**  (**5 nM**) |  |  | 140 pM |
| (Whitaker et al., 2001) | Carrier-free recombinant VEGF165 | Human VEGFR2 | Radioligand  (Saturation analysis; Not Scatchard) | **VEGF165**  R&D Systems  **VEGFR2**  COS-1 cells transiently transfected with human VEGFR2 cDNA | ? | ? | 339120 pM |
| **VEGF165**  R&D Systems  **NRP1**  Balb/c cells transiently transfected with human VEGFR2 cDNA | ? | ? | 291±54.36 pM |
| (Waltenberger et al., 1994) | Recombinant 125I-VEGF165 expressed in baculovirus system | Human VEGFR2 on PAE cells or HUVECs | Radioligand  (Scatchard analysis) | Porcine aortic endothelial **(PAE) cells** transfected with a VEGFR2-expressing vector | ? | ? | 760 pM |
| **HUVECs** | 770 pM |
| (Papadopoulos et al., 2012) | VEGF165 | Human  VEGFR1-hFc§ | SPR | **VEGF165**  Made at Regeneron Pharmaceuticals  **Human VEGFR1-hFc**  Obtained from R&D systems | 1.52±0.05×107 | 1.35±0.06×10-3 | 88.8±6.87 pM |
| (Cunningham et al., 1999) | VEGF165  (**0.625, 1.25,**  **2.5, 5 nM**) | Recombinant VEGFR2 Fc\* | SPR | **VEGFR2**  SF21 cells expressing VEGFR2 Fc or cbu |  |  | pM |
| VEGF165  (**1.14, 2.28,**  **4.55, 6.83 nM**) | Recombinant VEGFR2 cbu§ |  |  | pM |
| VEGF165  (2.5, 5, 10, 20 nM) | First three immunoglobulin-like domains of VEGFR2 | 4.72±1.0×106 | 0.67±0.11×10-4 | 14.5±1.0 pM |
| (Mamer et al., 2020) | Recombinant VEGF165  (**10, 20, 40nM**) | Immobilized recombinant VEGFR2 protein | SPR | Obtained from R&D Systems |  |  | pM |
| (Teran & Nugent, 2019) | Recombinant VEGF165 | Immobilized VEGFR2 Fc\* chimera | SPR | Obtained from R&D Systems |  |  | nM |
| (Rouet et al., 2005) | Recombinant 125I-VEGF165 | VEGFR2-Fc chimera† | ELISA plate+Saturation analysis  (Scatchard) | **VEGF165**  expressed in Sf9 insect cells  **VEGFR2**  R&D Systems | ? | ? | 292.5±163.8  pM |
| (Terman et al., 1992) | Recombinant 125I-VEGF165 | VEGFR2 on CMT-3 cells | Radioligand  (Saturation analysis; Scatchard) | **VEGF165**  Cells transfected with an expression vector containing the VEGF cDNA encoding the 165 amino acid form of VEGF  **VEGFR2**  CMT-3 monkey kidney cells transfected with KDR gene | ? | ? | 75 pM |
| (Lu et al., 2023) | Recombinant VEGF165 | Recombinant VEGFR2 | SPR | **VEGF165**  PeproTech  **VEGFR2**  R&D Systems | 3.58±1.44×107 | 4.13±0.28×10-3 | 115±73.4 pM |
| In-house data, 2023 | Recombinant VEGF165 | Recombinant VEGFR2 | SPR | **VEGF165**  R&D Systems  **VEGFR2**  R&D Systems | 6.24±0.46×105 | 3.18±1.98×10-4 | 520±250 pM |
| (Soker et al., 1996) | Recombinant 125I-VEGF165 | VEGFR2 on HUVEC | Radioligand (Saturation analysis; Scatchard) | **VEGF165**  Sf-9 insect cells infected with a baculovirus-based vector expressing VEGF-165 cDNA | ? | ? | 7.5 pM |
| (Tessler et al., 1994) | 125I-VEGF165 | VEGFR2 on NIH-3T3 cells‡ | Radioligand (Saturation analysis; Scatchard) | **VEGF165**  Sf-9 insect cells infected with a baculovirus-based expression vector for VEGF165  **VEGFR2**  The DNA encoding the entire chimera was then subcloned into the pMFG expression vector and expressed in NIH-3T3 cells. | ? | ? | 19 pM |

\* Fc: pre-dimerized fusion protein

§ cbu: monomeric fusion protein

† The extracellular domain of VEGFR2

‡ a chimeric receptor containing the extracellular do- main of the VEGFR2receptor fused to the transmembrane and intracellular domains of the human c-fms receptor in NIH-3T3cells

* **VEGF165:NRP1 binding affinity**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | | **Ligand/receptor source** | **()** | **()** |  |
| (Yen et al., 2011) |  |  |  | |  |  |  | 312 pM |
| (Whitaker et al., 2001) | Carrier-free recombinant VEGF165 | Human NRP1 | Radioligand  (Saturation analysis; Not Scatchard) | | **VEGF165**  R&D Systems  **NRP1**  COS-1 cells transiently transfected with human NRP1 cDNA | ? | ? | 2.09 nM |
| **VEGF165**  R&D Systems  **NRP1**  Balb/c cells transiently transfected with human NRP1 cDNA | 417±124.8 pM |
| (Soker et al., 1996) | Recombinant 125I-VEGF165 | NPR1 on HUVEC | Radio-ligand (Saturation analysis; Scatchard) | No heparin | **VEGF165**  Sf-9 insect cells infected with a baculovirus-based vector expressing VEGF-165 cDNA | ? | ? | 200 pM |
| NRP1 on breast cancer cell  (MDA-MB-231) | 280 pM |
| +heparin | 270 pM |
| (Soker et al., 1998) | Recombinant 125I-VEGF165 | NRP1 on porcine aortic endothelial (PAE) cells | Radioligand  (Scatchard analysis) | | **VEGF165**  Sf-21 insect cells infected with recombinant baculovirus vectors  **NRP1**  PAE cells transfected with NRP1 cDNA | ? | ? | 320 pM |
| (Fuh et al., 2000) | Biotinylated VEGF165 | First 600 amino acids of **mouse** NPR-1 extracellular domain (ECD), which lacked C-terminal MAM domain (immobilized) | **SPR**  Low density  (350 RU) | | **NRP1**  Transfected D. melanogaster cells |  |  | 2,000 nM |
| **SPR**  High density  (1400 RU) | | 113 nM |
| **ELISA**  No heparin | | 120 nM |
| **ELISA**  Add heparin | | 25 nM |
| (Pan et al., 2007) | VEGF165 | Human sNRP1-Fc§   * Immobilized * Containing ECD * Without MAM domain | SPR  (Steady-state analysis) | | **VEGF165**  Purchased from R&D Systems  **sNRP1**  Transfected Chinese hamster ovary cells | ? | ? | 120 nM |
| (Teran & Nugent, 2019) | Recombinant VEGF165 | Immobilized **rat** NRP-1 Fc\* chimera | SPR | | Obtained from R&D Systems |  |  | nM |
| Immobilized **mouse** sNRP-1 monomer (only ECD of the mouse sequence) |  |  | nM |
| (Gu et al., 2002) | Recombinant 125I-VEGF165 | NRP1 on COS-1 cells | Radioligand  (Saturation analysis; Not Scatchard) | | **NRP1**  COS-1 cells transiently expressing the Npn-1 | ? | ? | 0.93±0.71 nM |
| (Rouet et al., 2005) | Recombinant 125I-VEGF165 | NRP1-Fc chimera† | ELISA plate+Saturation analysis (Scatchard) | | **VEGF165**  expressed in Sf9 insect cells  **NRP1**  R&D Systems | ? | ? | 246.4±135.1  pM |
| (Vintonenko et al., 2011) | Recombinant VEGF165 | Recombinant NRP1 | SPR | | **NRP1**  R&D Systems |  |  |  |
| (Hervé et al., 2008) | VEGF165 | Recombinant NRP1 | SPR | | **VEGF165**  R&D Systems  **NRP1**  Purchased from an unknown vendor | 1.88±0.53×106 | 3.18±0.85×10-3 | 1.69±1.83 nM |
| (Lu et al., 2023) | Recombinant VEGF165 | Recombinant NRP1 | SPR | | **VEGF165**  PeproTech  **NRP1**  R&D Systems | 5.55±2.33×107 | 8.05±2.65×10-3 | 0.15±0.06 nM |
| In-house data, 2023 | Recombinant VEGF165 | Recombinant NRP1 | SPR | | **VEGF165**  R&D Systems  **NRP1**  R&D Systems | 7.96±2.15×105 | 1.56±0.55×10-3 | 6.36±1.07 nM |
| (Gluzman-Poltorak et al., 2000) | VEGF165 | NRP1 | Radioligand  (Saturation analysis; Scatchard) | | **VEGF165**  produced in sF9 cells using appropriate baculoviruses  **NRP1**  transfected PAE cells with the pcDNA3/np-1 expression vector | ? | ? | 180 pM |
| (Parker et al., 2012) | AP-tagged VEGF164 | NRP1 | ELISA with NRP1 affinity plates | | **VEGF164**  ?  **NRP1**  ? | ? | ? | 3.0±0.2 nM |
| (Von Wronski et al., 2006) | VEGF165 | NRP1-Fc‡ | Radioligand  (Competitive assay) | | **VEGF165**  Amersham Biosciences  **NRP1**  R&D Systems | ? | ? | 700 pM |

\* Fc: pre-dimerized

§ Fc: sNRP1s constructs were cloned into the expression vector pRK5 either fused to the Fc portion of human IgG1 to facilitate affinity purification.

† The extracellular domain of NRP1

‡ Fc: the Fc domain of human immunoglobulin

* **VEGF165:NRP2 binding affinity**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | **Ligand/receptor source** | **()** | **()** |  |
| (Finley et al., 2011) |  |  |  |  |  |  | 1 nM |
| (Geretti et al., 2007) | 125I-VEGF165 | NRP2 expressed from PAE cells | Radioligand  (Saturation analysis) | **VEGF165**  Purchased from R&D Systems or Provided by National Cancer Institute  **NRP2**  PAE cells transfected with NRP2 cDNA | ? | ? |  |
| (Gluzman-Poltorak et al., 2000) | 125I-VEGF165 | Recombinant NRP2 (splice form a22) expressed from PAE cells | Radioligand  (Scatchard analysis) | **VEGF165**  SF9 cells infected with baculoviruses  **NRP2**  PAE cells co-transfected with the PECE/np-2(a17) or PECE/np-2(a22) expression vectors and the pBabePuro plasmid | ? | ? | 0.13 nM |
| (Parker et al., 2012) | AP-tagged VEGF164 | NRP2 | ELISA with NRP2 affinity plate | **VEGF164**  ?  **NRP2**  ? | ? | ? | 150±4 nM |

* **VEGF121:VEGFR1 binding affinity**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | **Ligand/receptor source** | **()** | **()** |  |
| (Yen et al., 2011) |  |  |  |  |  |  | 33 pM |
| (Mamer et al., 2020) | Recombinant VEGF121  **(10, 20, 40nM)** | Immobilized recombinant VEGFR1 protein | SPR | Obtained from R&D Systems |  |  | nM |
| (Teran & Nugent, 2019) | Recombinant VEGF121 | Immobilized VEGFR1 Fc\* chimera | SPR | Obtained from R&D Systems |  |  | nM |

\* Fc: pre-dimerized

* **VEGF121:VEGFR2 binding affinity**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | **Ligand/receptor source** | **()** | **()** |  |
| (Yen et al., 2011) |  |  |  |  |  |  | 100 pM |
| (Mamer et al., 2020) | Recombinant VEGF165  **(10, 20, 40nM)** | Immobilized recombinant VEGFR1 protein | SPR | Obtained from R&D Systems |  |  | nM |
| (Teran & Nugent, 2019) | Recombinant VEGF121 | Immobilized VEGFR2 Fc\* chimera | SPR | Obtained from R&D Systems |  |  | nM |
| (Papo et al., 2011) | VEGF121 | Immobilized recombinant VEGFR2 extracellular domain | SPR | Obtained from R&D Systems |  |  |  |

\* Fc: pre-dimerized

* **VEGF121:NRP1 binding affinity**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | **Ligand/receptor source** | **()** | **()** |  |
| (Pan et al., 2007) | VEGF | Human sNRP1-Fc†   * Immobilized * Containing ECD * Without MAM domain | SPR  (Steady-state analysis) | **VEGF121**  Purchased from PeproTech  **sNRP1**  Transfected Chinese hamster ovary cells | ? | ? | 220 nM |
| (Parker et al., 2012) | AP-tagged VEGF120 | NRP1 | ELISA with NRP1 affinity plate | **VEGF120**  ?  **NRP1**  ? | ? | ? | 22±1 nM |

* **VEGF121:NRP2 binding affinity**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | **Ligand/receptor source** | **()** | **()** |  |
| (Parker et al., 2012) | AP-tagged VEGF120 | NRP2 | ELISA with NRP2 affinity plate | **VEGF120**  ?  **NRP2**  ? | ? | ? | 23±1 nM |

* **VEGF-B:VEGFR1 binding affinity**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | **Ligand/receptor source** | **()** | **()** |  |
| (Olofsson et al., 1998) | mVEGF-B186 | VEGFR1 | Competitive binding assay  (Recombinant hVEGF-165) | High Five cells infected with mVEGF-B186 pFASTBAC1 virus, NIH 3T3/VEGFR1 cells | ? | ? | pM |

* **VEGF-B:NRP1 binding affinity**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | **Ligand/receptor source** | **()** | **()** |  |
| (Mota et al., 2022) | Immobilized  Full length VEGF-B167 | NRP1-b1 | SPR | NRP1-b1 from 2 L E.coli Rosetta | ? | ? | 36 |
| VEGF-B167 peptide | Immobilized NRP1-b1 |  |  | 0.39 |
| VEGF-B186 peptide |  |  | 9.55 |

* **PlGF:NRP1 binding affinity**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | **Ligand/receptor source** | **()** | **()** |  |
| (Hoffmann et al., 2013) | rhPlGF-2 | NRP1 | SPR | **rhPlGF-2**  Produced in human embryonic kidney cells (HEK293 EBNA) using cDNAs of full-length PlGF-2 (Met-1 to Arg-152)  **NRP1**  Extracellular domain, Phe-22 to Lys-644 from BD Biosciences | ? | ? | 100 nM |

* **VEGF-C:VEGFR2 binding affinity**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | **Ligand/receptor source** | **kon (M-1s-1)** | **koff (s-1)** | **Kd** |
| (Joukov et al., 1997) | △N△C  (VEGF-C mutant mimicking mature VEGF-C) | VEGFR2 | Radioligand  (Saturation assay) | **△N△C**  Purified from yeast *P.pastoris*  **VEGFR2**  Transfected porcine aortic endothelial (PAE) cells | ? | ? | 410 pM |
| (Mäkinen et al., 2001) | Human recombinant VEGF-C | Human VEGFR2-Ig† | SPR | **VEGF-C**  Purified from transfected cells  **VEGFR2**  Purified from transfected cells | 5.5⨉104 | 12.3⨉10-4 | 22 nM |

† VEGFR2-Ig: a chimeric protein consisting of the ligand-binding portion of the extracellular part of VEGFR-2, joined to the Fc domain of immunoglobulin (Ig) γ-chain

* **VEGF-C:VEGFR3 binding affinity**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **Receptor** | **Method** | **Ligand/receptor source** | **kon (M-1s-1)** | **koff (s-1)** | **Kd** |
| (Joukov et al., 1997) | △N△C  (VEGF-C mutant mimicking mature VEGF-C) | VEGFR3 | Radioligand  (Saturation assay) | **△N△C**  Purified from yeast *P.pastoris*  **VEGFR3**  Transfected porcine aortic endothelial (PAE) cells | ? | ? | 135 pM |
| (Mäkinen et al., 2001) | Human recombinant VEGF-C | Human VEGFR3-Ig† | SPR | **VEGF-C**  Purified from transfected cells  **VEGFR3**  Purified from transfected cells | 13.6⨉104 | 6.05⨉10-4 | 4.4 nM |
| VEGF-C156S‡ | 0.35⨉104 | 4.0⨉10-4 | 115 nM |
| (Leppänen et al., 2013) | D123A/Q130A double mutant of VEGF-C | Monomeric VEGFR3 ECD  (D1–7) | ITC | **All proteins**  expressed in Sf21 insect cells | ? | ? | 34 nM |
| C137A mutant of human VEGF-C | Monomeric VEGFR3 ECD  (D1–2) | ? | ? | 250 nM |
| Monomeric VEGFR3 ECD  (D1–3) | ? | ? | 140 nM |
| Monomeric VEGFR3 ECD  (D1–5) | ? | ? | 3.7 nM |
| Monomeric VEGFR3 ECD  (D1–7) | ? | ? | 5.6 nM |
| D5 double mutant 5EA of VEGFR-3 D1-5 | ? | ? | 12 nM |

† VEGFR3-Ig: a chimeric protein consisting of the ligand-binding portion of the extracellular part of VEGFR-3, joined to the Fc domain of immunoglobulin (Ig) γ-chain

‡ VEGF-C156S: a mutant generated by replacement of the second conserved Cys (Cys156) residue of the recombinant processed VEGF-C by a Ser residue

* **VEGFR1:NRP1 binding affinity (Coupling rate)**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **VEGFR1** | **NRP1** | **Method** | **VEGFR1 source** | **NRP1 Source** |  | **()** |  |
| (Yen et al., 2011) |  |  |  |  |  |  |  |  |
| (Fuh et al., 2000) | VEGFR1 extracellular domain | NRP1 extracellular domain | SPR | Chinese hamster ovary (CHO) cells | Transfected *D. melanogaster* cells |  |  | 1.8 nM |

* **VEGFR2:NRP1 binding affinity (Coupling rate)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Protein** | **Method** | **Source** |  | **()** |  |
| (Yen et al., 2011) | VEGFR2:NRP1 |  |  |  |  | - |
| Mac Gabhann, 2005  (Mac Gabhann & Popel, 2005) | VEGFR2:NRP1 | Calculate the diffusion-limited rate and set it as the coupling rate |  |  |  | - |
| (Whitaker et al., 2001) | Human VEGFR2:NRP1 | Competition binding assay | COS-1 cell transfected with either VEGFR2 or NRP1 cDNAs, or both |  |  |  |
| (Dembo et al., 1982) | [IgE2:Fc]:Fc  (IgE2: dimerized IgE) | Calculate from   1. : Rate constant of crosslinking 2. : Experimentally determined (estimated by fitting ODE to histamine release level (%)) 3. : Initial number of free Fc receptors per cell (measured) 4. : Surface area of the basophil (Dembo *et al.*, 1979a) | **IgE**  Human IgE myeloma protein  **Fc receptors**  Human basophils |  | ? | - |

* **Protein-protein dimerization rate**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Protein** | **Method** | **Source** |  | **()** |  |
| (Mamer et al., 2019) | Arbitrary receptors | Assumed  (ODE system) | - |  |  | - |
| (Dijkman et al., 2018) | Rat NTS1† mutant fluorescently labelled at the intracellular end of TM4  (Cy3 and Cy5) | Single-molecule Förster resonance energy transfer (smFRET) | Expressed in *E. coli* BL21 as a fusion construct NTS1BH6‡ | () | 0.575 | - |
| (Moore et al., 1999) | Recombinant humanized  anti-VEGF | Dissociation experiment  (Fit to the plot of the concentration of dimer vs. time) | Purified from Chinese hamster ovarian cells |  |  | 0.91–350 µM |
| (M. J. Chen & Mayo, 1991) | Human Platelet factor 4 (PF4) | Saturation-transfer 1H Nuclear Magnetic Resonance (ST H NMR)  & Spin-Lattice Relaxation | Outdated human platelet |  |  | 147–500 µM |
| (Patapoff et al., 1993) | Recombinant human growth hormone (hGH) | Size exclusion high-performance liquid chromatography | Lyophilized recombinant hGH obtained from Genentech, Inc. |  |  | 2.6 µM |
| (Darke et al., 1994) | HIV-1 protease | Fit to the fluorescence change of an active-site-directed fluorescent probe upon its binding to HIV-1 protease | Expressed in *Escherichia coli* |  | 0.025 |  |

† Class A GPCR neurotensin receptor 1

‡ NTS1 is truncated at the N-terminus (1–42), has a hexa-His- tag added to its C-terminus, and is flanked by TEV protease recognition sites separating it from its N- and C-terminal fusion partners, maltose binding protein and thioredoxin, respectively, followed by an additional C-terminal deca-His-tag.

* **VEGFR internalization**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Receptor status** | **Data source** | **Data** | **Model** | **Method** | **Receptors** | **Value** |
| (Mac Gabhann & Popel, 2004) | Constitutive (free) | Wang, 2002 | The time courses of 125I-labeled VEGF internalization  (% 125I-VEGF bound on cell surface) | PDE for binding of VEGF and PlGF to VEGFR1/2 on endothelial cells | Apply a simplified version of the PDE model for a single growth factor and single receptor population to data | Either VEGFR1 or VEGFR2 | (assumption) |
| Bound |  |
| (Tan et al., 2013a) | Constitutive (free) | * (Lamalice *et al*., 2006) * (Chabot *et al*., 2009) * (Schneeweis *et al.*, 2010) * (Bruns *et al*., 2010) * (Zhang *et al*., 2010) | The time courses of   * # and normalized phosphorylated VEGFR2 * # and normalized phosphorylated Akt | ODE for Gab1/2-dependent VEGFR2 pathway to Akt activation | Estimate internalization rate | VEGFR2 |  |
| Bound |  |
| (Tan et al., 2013b) | Constitutive (free) | * (Lamalice *et al*., 2006) * (Chabot *et al*., 2009) * (Bruns *et al*., 2010) * (Zhang *et al*., 2010) | The time courses of   * # and normalized phosphorylated VEGFR2 * # and normalized phosphorylated Akt | ODE for VEGFR2 pathway to ERK activation | Estimate internalization rate | VEGFR2 |  |
| Bound |  |
| (Weddell & Imoukhuede, 2017) | Unphosphorylated | * **ICAM-1**:   Muro *et al.*, 2003  Muro *et al.*, 2004   * **VEGFR2**: Lampugnani *et al.*, 2006 * **EGFR**:   Danglot *et al.*, 2010   * **Heparin sulfate and integrin**:   Greene *et al.*, 2012 | * % Total internalized receptors * % Total receptors localized to the nucleus * % Total receptors co-localized with early endosomes * Receptor localization with early endosomes over time * % Total receptor co-localization with late endosomes * Receptor co-localization with late endosomes over time | ODE for RTK endocytosis signaling | Estimate RTK-specific internalization rate for the receptors and get a generalized rate | * VEGFR1 * VEGFR2 * IGFR1 * FGFR1 * EFGFR * PDGFRα * PDGFRβ * Tie2 |  |
| Phosphorylated |  |
| Dissertation:  (Castleberry, 2022) | Constitutive (free) | Wang, 2002 | The time courses of 125I-labeled VEGF internalization  (% 125I-VEGF bound on cell surface) | ODE for cross-family binding interactions | Approximating a first-order reaction rate from data | VEGFR1 or VEGFR2 |  |
| Bound |  |
| (Sarabipour, 2022)  Submitted | Constitutive (free) | Experiment on HUVECs | * Whole-cell VEGF receptors expression levels in the absence of exogenous ligands * Localization patterns (cell surface vs intracellular) * Whole-cell VEGF receptors expression levels when inhibiting recycling pathways (with or without CHX) | ODE for trafficking of VEGFR1, VEGFR2, and NRP1 on HUVECs  (no nucleus) | Estimate internalization rate for VEGFR1, VEGFR2, and NRP1 based on experimental measurements | VEGFR1 |  |
| VEGFR2 |  |
| NRP1 |  |
| (Wang et al., 2002) | Bound | HUVEC | The time courses of 125I-labeled VEGF internalization  (% 125I-VEGF bound on cell surface) |  | Estimate internalization rate, , using the first-order equation | VEGFR1  VEGFR2 NRP1 |  |

* **VEGF:GAG binding**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **GAG** | **Method** | **Source** | **()** | **()** |  |
| (Yen et al., 2011) |  |  |  |  |  |  | 24 nM |
| (Filion & Popel, 2004) |  |  |  |  |  |  | 1.03 nM |
| (Nugent & Edelmant, 1992) | Recombinant basic fibroblast growth factor (bFGF) | HSPG | Radioligand  (Direct target-ligand binding;  Curve fitting to time-course for association and dissociation) | **bFGF**  From Chiron Inc.  **HSPG**  Mouse Balb/c3T3-produced extracellular matrix coated tissue (only HSPG) |  |  | 1.03 nM |
| (Lim et al., 2016) | Recombinant VEGF165a | Heparan sulfate | SPR | **VEGF165a**  Obtained from R&D Systems |  |  | 3.3 nM |
| (Martino et al., 2014) | VEGF-A165 | HS | **ELISA**   1. Heparin-binding plates (BD Bioscience) were coated with 25 μg/ml of heparan sulfate   The binding curve was fitted by non-linear regression to obtain the dissociation constant (KD) using A450 nm = Bmax\*[GF]/(KD + [GF]). | **VEGF-A**  Invitrogen  **HS**  Sigma-Aldrich | ? | ? | 60.9±9.7 nM |

* **PlGF:GAG binding**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **GAG** | **Method** | **Source** | **()** | **()** |  |
| (Martino et al., 2014) | PlGF-2 | HS | **ELISA**   1. Heparin-binding plates (BD Bioscience) were coated with 25 μg/ml of heparan sulfate   The binding curve was fitted by non-linear regression to obtain the dissociation constant (KD) using A450 nm = Bmax\*[GF]/(KD + [GF]). | **PlGF-2**  PeproTech  **HS**  Sigma-Aldrich | ? | ? | 4.6±0.4 nM |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |

* **PDGF:GAG binding**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Ligand** | **GAG** | **Method** | **Source** | **()** | **()** |  |
| (Finley et al., 2011) | VEGF | GAG |  |  |  |  | 24 nM |
| (Söderlund et al., 2022) | PDGF-AA | GAGnr3 | 1. GAGs were chemoenzymatically produced by adding one sugar molecule at a time with purification in between. 2. The synthetic glycosaminoglycan was built on an azide backbone, which was printed on a cyclic alkyne microscope slide using a pipetting robot. 3. Use **SPR** to measure binding affinities. | **GAG**  Synthesized  **PDGF-AA**  R&D systems |  |  | 45.6 nM |
| GAGnr10 |  |  | 28.2 nM |
| GAGnr19 |  |  | 12.9 nM |
| GAGnr26 |  |  | 27.8 nM |
| GAGnr34 |  |  | 21.5 nM |
| GAGnr43 |  |  | 32.5 nM |
| (Goretzki et al., 1999) | PDGF-AA | D2¶ | **ELISA**  Growth Factor Binding to Immobilized NG2  Dissociation constants were determined by nonlinear regression analysis. | **NG2 (CSPG)**  Purified and produced recombinant fragments  **PDGF-AA**  R&D Systems | - | - | 13.2±2.4 nM |
| D3§ | - | - | 9.3±1.0 nM |
| EC with GAG chains† | - | - | 15.3±4.9 nM |
| EC without GAG chains‡ | - | - | 10.0±3.5 nM |
| D2 | **SPR**   1. Each ligand was immobilized at a concentration of approximately 1500 resonance units (1.5 ng/mm2). 2. The association and dissociation phases of the sensorgrams were fit simultaneously, assuming a simple bimolecular reaction model: A + B ↔ AB. |  |  | 25.9 nM |
| D3 |  |  | 22.8 nM |
| EC with GAG chains |  |  | 40.1 nM |
| EC without GAG chains |  |  | 30.4 nM |
| (Martino et al., 2014) | PDGF-BB | HS | **ELISA**   1. Heparin-binding plates (BD Bioscience) were coated with 25 μg/ml of heparan sulfate 2. The binding curve was fitted by non-linear regression to obtain the dissociation constant (KD) using A450 nm = Bmax\*[GF]/(KD + [GF]). | **PDGF-BB**  PeproTech  **HS**  Sigma-Aldrich | ? | ? | 42.3±6.3 nM |
| (Gohring et al., 1998) | PDGF-AA | Core protein of Perlecan (HSPG) | **SPR**   1. Surface plasmon resonance assays were performed with BIAcore 1000 instrumentation. 2. Immobilizations resulted in 2000–7000 RU (perlecan and its fragments). 3. Kinetic constants were calculated by non-linear fitting of the association and dissociation curves according to the 1 : 1 model A1B 5 AB using BIAevaluation software version 2.1. | **PDGFs**  Amgen  **Perlecan**  Mouse Engelbreth- Holm-Swarm tumor | 3.4×104 | 0.78×10-3 | 23 nM |
| PDGF-BB | 2.4×105 | 0.78×10-3 | 3 nM |

¶ D2: a subdomain of NG2, containing GAG chains

§ D3: a subdomain of NG2, without GAG chains

†EC with GAG chains: NG2/EC (extracellular) with GAG chains

‡EC without GAG chains: NG2/EC (extracellular) without GAG chains, comprising the whole extracellular domain (residues 1–2223)

* **VEGF-A clearance**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Species** | **Status** | **Sex** | **Protein** | **Protein source** | **Data** | | **Method** | **Value ()** |
| (Eppler et al., 2002) | Human | Patients with coronary artery disease | Both | rhVEGF165 | ? | **Mean (SD) VEGF plasma concentration vs. time** | 17 ng/kg/min | Non-compartment model |  |
| 50 ng/kg/min | Non-compartment model |  |
| Dose-independent | Fit a mechanism-based, target-mediated drug distribution model to data |  |
| (George et al., 2015) | C57Bl/6 mice | ? | ? | VEGF121 | From ProSpec | **Mean VEGF121 plasma concentration vs. time**   1. Inject 123 nmol/kg of VEGF121 in the femoral artery. 2. Sample blood repeatedly for 4 hours. | | Fit a two-compartment pharmacokinetic model to data |  |

* **VEGF-B clearance**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Species** | **Status** | **Sex** | **Protein** | **Protein source** | **Data** | **Method** | **Value ()** |
|  |  |  |  |  |  |  |  |  |

* **PlGF clearance**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Species** | **Status** | **Sex** | **Protein** | **Protein source** | **Data** | **Value (t1/2)** |
| (Y. Tan et al., 2022) | Rat | ? | ? | PlGF | **Aggamin**  cDNA encoding human PlGF131 cloned into an expression vector and electroporated into Chinese Hamster Ovary cells | **PlGF is intravenously administered**   1. Rat: 200 and 500 μg/kg doses 2. Pregnant Guinea pigs: 130 and 430 μg/kg doses 3. Cynomolgus monkeys: 100 and 300 μg/kg doses | 3.1-3.9 hr |
| Hartley Guinea pigs | Pregnant | Female | 2.2-2.3 hr |
| cyno- molgus monkey | ? | ? | 1.3-3.0 hr |

* **PDGF clearance**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Species** | **Status** | **Sex** | **Protein** | **Protein source** | **Data** | **Method** | **Value ()** |
| (Bowen-Pope et al., 1984) | Baboon | Healthy | ? | 125I-PDGF | **PDGF**  Prepared by authors | **Time vs. fraction of total TCA-insoluble radioactivity recovered per milliliter of plasma sample**   1. The solution containing radiolabeled protein was injected into the brachiocephalic vein. 2. At timed intervals after injection, samples of blood were drawn into EDTA from peripheral venous sites on a rotating basis, excluding the injection site. 3. Blood was drawn into a mixture of inhibitors of platelet activation. 4. Total radioactivity in a l-mL sample was determined by gamma-spectrophotometry. | Fit to three-compartment model | 0.041±0.009 |
| Pure PDGF | 1. 2.5 µg of purified PDGF mixed with 4.0 ng 125I-PDGF in 3.0 mL 20% baboon plasma in PBS was injected into each of two adult male baboons. 2. Samples were withdrawn in prechilled syringes containing the mixture of inhibitors of platelet alpha-granule release. 3. The resulting plasma was analyzed for TCA-insoluble radioactivity and for PDGF detectable by radio-receptor assay (RRA). 4. The contribution of plasma 125I-PDGF to total 125I-PDGF binding in the RRA for PDGF content was determined from parallel cultures to which no additional 125I-PDGF was added and was found to be too small to affect the assay results. 5. The plasma levels of TCA-insoluble radioactivity and of radioreceptor assayable PDGF are expressed as percent of the value that would be obtained if all injected PDGF and 125I-PDGF were to become distributed in the subject’s entire plasma volume. | | t1/2=1.9±0.5 min |
| (Santhini et al., 2022) | ? | ? | ? | PDGF | ? | ? | | t1/2=30 min |
| (Abdiu et al., 1998) | BALB/cA-nu/nu mice | 6- to 12-week old, congenitally dysthymic | Male | 125I-PDGF-AB | **PDGF-AB**  Gift from Ludwig Institute for Cancer Research | 1. Three series of mice, 12 mice in each, were given 250,000 cpm 125I-PDGF-AB per animal, by either of the following routes of administration (**extravascular**): intraperitoneal injection; intramuscular injection in the upper thigh; or subcutaneous injection on the back. 2. Blood samples of about 1 ml were collected at various times within 24 hours 3. Radioactivities of blood samples and prepared sera were measured by gamma- spectrometry 4. In order to analyze the proportion of macromolecular to low-molecular 1251precipitation with 10% trichloroacetic acid (TCA) was done. | | **Plasma**  t1/2=4.5 h |
| **Injection site**  0.023 min-1 |
| (Cohen et al., 1990) | Sprague-Dawley rats | ? | Male | 125I-PDGF-BB | **PDGF-BB**  From amersham | 1. Male Sprague-Dawley rats (250-300 g) were injected with 125I-labeled recombinant human PDGF-BB (2.5 &i/35 @g/kg) via the lateral tail vein. 2. At intervals between 5 min and 2-hour, blood samples were withdrawn from an indwelling carotid artery catheter. 3. Total radioactivity in the sample was determined with a gamma counter. 4. Plasma clearance kinetics of TCA-in- soluble radioactivity were estimated using a two-compartment, nonlinear regression model. | | t1/2=5.2 min |

* **VEGF degradation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Reference** | **VEGF source** | **Used cell or complex** | **Method** | **Value ()** |
| (Kleinheinz et al., 2010) | Recombinant human VEGF165 | Equine (horse) collagen complex charged with VEGF165 | 1. The complexes were charged with VEGF165 in three different complexes: 0.8 µg, 10 µg, 80 µg. 2. The complexes were incubated for 5 days. 3. VEGF dissolution in aqueous solution was analyzed repeatedly. |  |
| (R. R. Chen et al., 2007) | VEGF165 from Biological Resources Branch of the National Cancer Institute | Incubated with dermal microvascular endothelial cells (MECs) | 1. VEGF was incubated with MECs *in vitro*. 2. Measure % of total bioactivity of VEGF. 3. Calculate the half-life of VEGF based on the time required for VEGF to lose half its bioactivity. |  |
| (Serini et al., 2003) | Recombinant human VEGF165 | Human endothelial cells | 1. VEGF-A165 and 10 nCi of 125I-VEGF were incubated for different intervals of time with EC plated on Matrigel. 2. VEGF-A was immunoprecipitated from the medium with a polyclonal anti-VEGF-A antibody. 3. Radioactivity corresponding to the VEGF-A band in SDS±PAGE (12%) was counted and used to calculate the half-time by EnzFitter software |  |

**Chart, line chart

Description automatically generated**

* **Microvascular permeability**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Reference** | **Subject** | **Location** | **Method** | **Treatment** | **Value** |
| (Stefanini et al., 2008) | Human |  | Deduced from (Garlick & Renkin, 1970) (considered VEGF’s hydrodynamic radius) |  | cm/s |
| (Garlick & Renkin, 1970) | Mongrel dog | Paw | 1. Cannulate lymphatics from the lower leg and paw before they entered the popliteal node. 2. Place a centrally directed cannula in a popliteal lymphatic in the paw in one experiment, and a peripherally directed cannula in the same lymphatic just distal to the popliteal node, and directed an infusion of an artificial lymph solution centrally through the paw cannula at a rate about 0.05 ml/min. The solution contains dextran 10 and sucrose-14C. 3. The effluent from the popliteal cannula is collected as for lymph and compared with the infusate with respect to volume and concentration of the two test molecules. |  | mL/s |
| (Lal et al., 2001) | Passage 1 HUVEC from Clonetics | - | 1. The diffusion system contained six units, with each unit having two chambers. 2. The chamber whose lumen faced the HUVEC was defined as the luminal chamber (LC), and HUVEC-devoid side of the membrane was defined as the abluminal chamber (ALC). 3. The medium in each LC was replaced with 5 ml of warm serum-free EBM containing 13.3 mg/ml FITC-labeled dextran (70 kDa). Baseline EC layer permeability (*P*) was then measured for 60 min. 4. Recombinant human VEGF165 was added to both chambers at time 60 min and additional measurements were per- formed for the next 60 min. 5. Permeability was calculated by measuring fluorescence intensity as a function of time according to the standard formula: P = J/A△C, where P=permeability; J=solute flux; A=area of membrane; and △C=concentration difference across the diffusion membrane | No treatment  (13.3 mg/ml FITC-labeled dextran) | cm/s |
| VEGF 0.034 nM | ? |
| VEGF 0.068 nM | ? |
| VEGF 1 nM | cm/s |
| VEGF 10 nM | ? |
| VEGF 100 nM | ? |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Diet or transgenic** | **Sex** | **Age** | **Location** | **Method** | **Value** |
| (Algenstaedt et al., 2003) | Mouse | Normal | Both | 20 wk. | Skin | 1. Dorsal skin-fold chambers were implanted exposing subcutaneous tissue and striated skin muscle. 2. To obtain microcirculatory parameters, randomly selected areas were investigated using a fluorescence microscope. 3. After the injection of TRITC-labeled BSA, the fluorescence intensity was measured intermittently for 25 min and recorded digitally. 4. The value of P was calculated as P=(1-HT)\*V/S\* [1/(I0-Ib)\*dI/dt+1/K], where I is the average fluorescence intensity of the whole image, I0 is the value of I immediately after the filling of all vessels by TRITC-BSA, Ib is the background fluorescence intensity, and HT is the amount of hematocrit. V and S are the total volume and surface area, respectively, of vessels within the tissue volume covered by the surface image. The time constant of BSA plasma clearance (K) is 9.1⨉103 s. | cm/s |
| UCP1/DTA (genetically obese) | Both | cm/s |
| (Sarelius et al., 2006) | Mouse  (C57Bl/J) | Normal | Male | ? | Cremaster muscle arterioles | 1. The right cremaster muscle was surgically exteriorized with the aid of a dissecting microscope. 2. The feed vessel to the microvascular network was cannulated and perfused with fluorescent-labeled BSA prepared. 3. Solute permeability, Ps, was measured in either an arteriole or a venule, occasionally in both. 4. The total fluorescence intensity was measured for the region of interest. 5. The imaged confocal slice of tissue was calculated to be 15 m in depth for the 10⨉ objective. | cm/s |
| Cremaster muscle venules | cm/s |
| Sprague-Dawley Rat | Normal | Male | ? | Abdominal wall muscle arterioles | 1. Selected vessels (either arterioles or venules) were cannulated with a sharply beveled double-barreled glass micropipette that contained an unlabeled washout solution (10 mg/ml BSA in Krebs) in one-half of the theta pipette and BSA-488 in Krebs in the other half of the pipette. 2. The total fluorescence intensity was measured for the region of interest. 3. The imaged confocal slice of tissue was calculated to be 15 m in depth for the 10⨉ objective. | cm/s |
| Abdominal wall muscle venules | cm/s |

* **Lymphatic drainage flow rate**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Sex** | **Diet** | **Location** | **Method** | **Value** |
| (Arngrim et al., 2013) | Human | Male | Lean | Subcutaneous adipose tissue | 1. To measure ATLD, 99mTc-albumin-nanocolloid with a mean radius of 6–8nm was used. 2. A volume of 1MBq Nanocoll in 0.1ml isotonic sodium chloride was injected intradermally into the lower left-abdominal quadrant. 3. The washout rate was measured continuously with a scintillation-counting device. | /min |
| Obese | /min |

* **GAG binding site**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Sex** | **Diet** | **Location** | **Method** | **Value** |
| (Yoon et al., 2023) | Adult C57BL/6 mice | Female | Obese | Subcutaneous inguinal AT | 1. Decellularize the AT 2. Measure GAG content | 0.29±0.017 µg/mg tissue |
| Lean vs. Obese | For protein identification, liquid chromatography-tandem mass spectrometry (LC-MS/MS) of native AT and AT dECM was performed using the shotgun method. | GAG ratio = 1:5 for lean vs. obese mice  HSPG2 among proteoglycan: 7% in obese mice  HSPG2 among proteoglycan: 11% in lean mice  HSPG2 ratio=3:2 for lean vs. obese mice |

* **Lymph flow rate**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Animal** | **Sex** | **Diet** | **Location** | **Method** | **Value** |
| (Trevaskis et al., 2020) | Human | Male | - | Thoracic duct | 1. Thoracic lymph fluid was collected from three male patients via a 5 Fr cholangiography catheter inserted into the thoracic lymph duct during an Ivor Lewis oesophagogastrectomy to resect an adenocarcinoma of the distal esophagus. 2. The patients were fasted before surgery and for 24 h after surgery. They then received Nutrison standard (3.9 g/dL total fat with 1 g/dL saturated fat, 2.2 g/dL monounsaturated fat and 0.7 g/dL polyunsaturated fat) feed via the proximal jejunum at different rates. 3. Lymph flow rate was determined gravitrimetrically. | ml/h/kg |
| Greyhound dog | Male | - | Thoracic lymph | 1. Dogs were fasted overnight and for 12 h post-dose and administered a single (1 g) soft gelatin capsule containing 1.6 mg/kg halofantrine in 18.1 mg/kg long chain lipid in a SEDDs formulation. 2. Alternatively, the dogs were fasted or fed a can of commercial dog food containing ∼1000 mg/kg of fat 30–45 min prior to administration of 100 mg halofantrine base in standard tablet formulations. 3. After formulation administration the lymph fluid was collected continuously. 4. Data for 0–8 h following commencement of formulation administration was analyzed. 5. Lymph flow rates were determined gravitrimetrically. | ml/h/kg |
| Sprague- Dawley rat | Male | - | Mesenteric lymph | 1. The rats were infused with halofantrine lipid formulations at a rate of 2.8 ml/h for 2 h. 2. After formulation administration the lymph fluid was collected continuously. 3. Data for 0–8 h following commencement of formulation administration was analyzed. 4. Lymph flow rates were determined gravitrimetrically. | ml/h/kg |
| C57BL/6 mouse | Male | - | Mesenteric lymph | 1. The mice were administered formulations into the duodenum over 1 h consisting of 1.6 mg/kg halofantrine and 18.1, 250, or 1000 mg/kg oleic acid dispersed in 0.5 ml of 0.2% Tween 80 in normal saline. 2. After formulation administration the lymph fluid was collected continuously. 3. Data for 0–8 h following commencement of formulation administration was analyzed. 4. Lymph flow rates were determined gravitrimetrically. | ml/h/kg |

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