VEGF refs- continuous list

Project purpose: To determine whether there is a correlation between isoforms of VEGF proteins, corresponding blood vessel proliferation and possible optimization of monoclonal antibody/VEGF trap drugs in treating Wet-AMD.

NOTE- the list below is not my official reference list, this is a compilation of references I used to build background knowledge before beginning the project the section labelled “VEGF refs- Used refs” is my official reference list.

[1]Wet Macular Degeneration: Symptoms & Treatment
[2]Understanding Macular Degeneration - American Academy of Ophthalmology
[3]What Is the Role of Ischemia in AMD? | Retinal Physician.
[4]AMD REF- Exudative versus Nonexudative Age-Related Macular Degeneration: Physiopathology and Treatment Options - PMC - 3.2- use for wet AMD refs abt treatment with antiangiogenic drugs
[5]https://emedicine.medscape.com/article/1226030-treatment?form=fpf
[6]The heparin-binding domain confers diverse functions of VEGF-A in development and disease: a structure-function study - PubMed.
[7]Heparin-Binding Domains in Vascular Biology - PMC
[8]Heparin and Heparan Sulfate: Analyzing Structure and Microheterogeneity - PMC
[9]Heparan sulphate and heparin interactions with proteins | Journal of The Royal Society Interface
[10]Disulfide structure of the heparin-binding domain in vascular endothelial growth factor: characterization of posttranslational modifications in VEGF - PubMed
[11]Frontiers | Heparan Sulfate: A Ubiquitous Glycosaminoglycan with Multiple Roles in Immunity
[12]Heparan Sulfate Proteoglycans - PMC
[13]Comparison of Anti-VEGF Treatments for Wet AMD - American Academy of Ophthalmology
[14]Protein Isoform - an overview | ScienceDirect Topics “It is known that alternative splicing of mRNA results in mRNA transcripts and proteins of different isoforms, and that different forms of proteins may have drastically different properties as the protein structure as well as its domain compositions may be directly or indirectly affected..”
[15]Plasmin - an overview | ScienceDirect Topics.
[16]VEGF-A mRNA processing, stability and translation: a paradigm for intricate regulation of gene expression at the post-transcriptional level | Nucleic Acids Research | Oxford Academic
[17]New Insights into VEGF-A Alternative Splicing: Key Regulatory Switching in the Pathological Process
[18]Targeting VEGF in eye neovascularization: What's new?: A comprehensive review on current therapies and oligonucleotide-based interventions under development - ScienceDirect
[19]Vascular Endothelial Growth Factor (VEGF) and Its Receptor (VEGFR) Signaling in Angiogenesis: A Crucial Target for Anti- and Pro-Angiogenic Therapies - PMC

[20]Isoform-specific expression of VEGF-B in normal tissues and tumours - PubMed
[21]Vascular Endothelial Growth Factor Receptor-2 and Neuropilin-1 Form a Receptor Complex That Is Responsible for the Differential Signaling Potency of VEGF165 and VEGF121 - ScienceDirect
[22]VEGF121, a Vascular Endothelial Growth Factor (VEGF) Isoform Lacking Heparin Binding Ability, Requires Cell-surface Heparan Sulfates for Efficient Binding to the VEGF Receptors of Human Melanoma Cells* - Journal of Biological Chemistry
[23]The vascular endothelial growth factor (VEGF) isoforms: differential deposition into the subepithelial extracellular matrix and bioactivity of extracellular matrix-bound VEGF. | Molecular Biology of the
Cell.
[24]The vascular endothelial growth factor (VEGF) family: angiogenic factors in health and disease | Genome Biology | Full Text
[25]Vascular Endothelial Growth Factor (VEGF) and Its Role in Non-Endothelial Cells: Autocrine Signalling by VEGF - Madame Curie Bioscience Database - NCBI Bookshelf
[26]The PDGF family: four gene products form five dimeric isoforms - PubMed
[27]VEGF111: new insights in tissue invasion - PMC
[28]Protein Degradation - The Cell - NCBI Bookshelf.
[29]7.19F: Proteolytic Degradation - Biology LibreTexts.
[30]What is RNA splicing?
[31]Biochemistry, Primary Protein Structure - StatPearls - NCBI Bookshelf.
[33]A model for isoform-level differential expression analysis using RNA-seq data without pre-specifying isoform structure - PMC.
[34]Mass Spectrometry-Based Protein Sequencing - Creative Proteomics
[35]Mass Spectrometer - StatPearls - NCBI Bookshelf
[36]Protein Mass Spectrometry
[37] mass spectrometry - How long does it take to run an MS/MS experiment - Chemistry Stack Exchange
[38]Resources | SAMS | Southern Alberta Mass Spectrometry Facility | Cumming School of Medicine | University of Calgary
[52]Mass spectrometry and amplification of VEGF by PGF.(a,b) Mass... | Download Scientific Diagram
[39]Aflibercept - StatPearls - NCBI Bookshelf
[40]Zaltrap.
[41]Aflibercept in the treatment of patients with metastatic colorectal cancer: latest findings and interpretations - PMC
[42]Brolucizumab - EyeWiki
[43]The Expanding Role of Vascular Endothelial Growth Factor Inhibitors in Ophthalmology - PMC
[44]What is mCNV? | LUCENTIS® (ranibizumab)
[45]Pegaptanib: Uses, Interactions, Mechanism of Action | DrugBank Online
[46]The carboxyl terminus of VEGF-A is a potential target for anti-angiogenic therapy - PMC

[48]https://www.health.tas.gov.au/health-topics/eyes-and-vision-ophthalmology/common-eye-disordersn
[49] 121 tumorigenesis- The 121 amino acid isoform of vascular endothelial growth factor is more strongly tumorigenic than other splice variants in vivo - PubMed
[50]189 tumorigenesis- Unique properties of 189 amino acid isoform of vascular endothelial growth factor in tumorigenesis - PubMed
Click on the image to zoom
[51]Pigment Epithelial Detachment - EyeWiki
[52]Monoclonal Antibodies (MABs)
[53]Monoclonal Antibodies: Definition & How Treatment Works
[54]Recent advances in anti-angiogenic inhibitors targeting VEGF/VEGFR axis - PMC
[55]https://pmc.ncbi.nlm.nih.gov/articles/PMC8910030/table/ijms-23-02592-t002/ Drug table from ref 4
[56]Tyrosine kinase – Role and significance in Cancer - PMC. This is the reference for when you're writing about VEGF receptors.
[57]VEGFR-1 and VEGFR-2: two non-identical twins with a unique physiognomy - PMC.
[58]New prospects in the roles of the C-terminal domains of VEGF-A and their cooperation for ligand binding, cellular signalling and vessel formation - PubMed
[59]VEGF-A splice variants bind VEGFRs with differential affinities - PMC
[60]The physiological and pathological functions of VEGFR3 in cardiac and lymphatic development and related diseases
[61]Molecular Pharmacology of VEGF-A Isoforms: Binding and Signalling at VEGFR2 - PMC.
[62]Direct measurements of VEGF–VEGFR2 binding affinities reveal the coupling between ligand binding and receptor dimerization - PMC.
[63]Mechanisms of activation of receptor tyrosine kinases: monomers or dimers - PubMed.
[64]CDD Conserved Protein Domain Family: Ig_VEGFR

Rewritten priority checklist

- ☐ 1) Study the mAbs and their characteristics alone, applications, structure, function, etc for all.
- ☐ 2) Study the characteristics of Aflibercept as a receptor decoy and study the recombinant activity.
- ☑ ~~3) Study the characteristics, pathology, etiology, physiology, diagnosing, current treatments and side effects of wet age-related macular degeneration + how mAbs are used in Wet-AMD.~~
- ☑ ~~4) Study genetic protein structure. Eg- C and N-terminus. DNA structure. Extracellular matrix, polypeptide amino acid structure, (later more specifically VEGF structure and amino acid composition). (Diagram for board?)~~

- [x] ~~5) Study VEGF in-depth and figure out the differences between isoforms, their characteristics, alternative splicing, and how common each isoform is (vascularization). Classify the exons/introns and their functions and how they affect the characteristics of an oncoming blood vessel. Specify the exon composition of all isoforms, including VEGF-111 + diagrams (For CYSF board)~~
- [ ] 6) Consecutively study the characteristics of Aflibercept as a receptor decoy and mAbs concerning the VEGF isoforms and the recombinant activity of the receptor decoy Aflibercept and mAbs.
- [ ] 7) Compare characteristics of isoforms to the binding capabilities of the mabs, bevacizumab (Avastin), and Ramucirumab (Cyramza), Brolucizumab (Beovu), Ranibizumab (Lucentis) and Aflibercept (Zaltrap). And study how vessels produced by different isoforms result in differentiated blood vessels with different side effects
- [ ] 8) Study the process of mass spectrometry full-length protein sequencing (cost, viability, risk control, Intravitreal injections for sample collecting, 5 Ws). (Diagram or 3D model or prototype for CYSF board??).
- [ ] 9)Medical applications of Wet-AMD isoform categorization treatment through mass spectrometry

Unordered project checklist

- [x] ~~Figure out the differences between isoforms and their characteristics. (vascularization)~~
- [x] ~~Classify the exons and their functions and how that affects the characteristics of an oncoming blood vessel.~~
- [x] ~~Determine the exon composition of all isoforms, not including VEGF-111 + diagrams (For CYSF board)~~
- [x] ~~Study genetic protein structure. Eg- C and N-terminus. DNA structure. Extracellular matrix, polypeptide amino acid structure~~
- [x] ~~Study the process of mass spectrometry full-length protein sequencing (cost, viability, risk control, Intravitreal injections for sample collecting, 5 Ws. (Diagram or 3d model or prototype for CYSF board??)~~
- [x] ~~Compare characteristics of isoforms to the binding capabilities of the 2 mabs, bevacizumab (Avastin), and Ramucirumab (Cyramza), Brolucizumab (Beovu), Ranibizumab (Lucentis)~~
- [x] ~~Compare the mabs to the clinical results of the use of aflibercept in wet age-related macular degeneration~~
- [x] ~~Study the characteristics of Aflibercept as a receptor decoy concerning the VEGF isoforms consecutively.~~
- [x] ~~Study the recombinant activity of the receptor decoy Aflibercept~~

- [x] ~~Compare the drugs to their VEGF isoform characteristics and then bind the drugs to the isoforms that create the vessels~~
- [x] ~~Study how vessels produced by different isoforms result in differentiated blood vessels with different side effects~~
- [x] ~~Study the characteristics, pathology, etiology, physiology, and side effects of wet age-related macular degeneration~~
- [x] ~~Medicinal applications of Wet-AMD isoform categorization treatment~~
- [x] ~~blueprint/model/diagram of a mass spectrometer (For board)~~

EMAIL-

My project aims to categorize the various VEGF isoforms, their characteristics, and their angiogenic potential for optimal treatment in W-AMD using monoclonal antibodies that target VEGF proteins. My project centers around Wet- AMD (Wet- Age-Related Macular Degeneration) which is a disease characterized by neovascularization in the eye near the macula. This abnormal blood vessel growth is generally weaker than other blood vessels and has a high likelihood of leaking proteins causing harm and degradation to the macula, lowering visual acuity and causing blindness The drugs I will be looking at are still not yet fully decided but I have a couple of options, at most 3 or 4. Brolucizumab, Bevacizumab, ramucirumab, and ranibizumab, are monoclonal antibodies that inhibit or bind to VEGF (A or B depending on the drug). Aflibercept, also called VEGF-trap, is a soluble decoy receptor, different from the mABs in its composition and treatment capabilities. VEGF (Vascular endothelial growth factor) is a primary protein for the production of blood in vessels. These drugs were originally prominent in cancer research, known for their capabilities in stripping tumours of their nutrient sources by inhibiting blood vessel growth and shrinking tumours. Most of these drugs are still off-label for use in ophthalmology. But, the issue here is not the drugs, but the VEGF protein. In many proteins, in their production from Pre-MRNA to proteins, they undergo a process called RNA splicing or a similar process called alternative splicing. Alternative splicing is when isoforms of the same protein will be produced because certain exons are skipped in the genetic code. Each exon codes for a different characteristic of the protein, so missing characteristics/exons will code for proteins that produce blood vessels that have varying qualities. For example, the only freely soluble non-heparin binding isoforms of VEGF are VEGF-121 and VEGF-111, both of which are missing their 6a and 6b exons. These exons code for the highly basic HBD, (Heparin-binding domain). This part of the protein allows the blood vessels produced not to clot by binding to heparin-sulfate, a natural anticoagulant with other features (present in most eukaryotic cells); it also allows them to bind to the coreceptor Nrp-1. Alternative splicing causes these exons to be skipped, and the resulting blood vessels lack these basic characteristics that are essential for their purpose. (Blood vessels produced by VEGF-121/111 generally are weaker and more prone to blood clots and have a higher likelihood of leaking because of their inability to bind to heparan-sulfate). In summary, my project will take the characteristics of drugs and their compositions and treatment abilities and match them to corresponding isoforms for optimal treatment enhancement with the goal of retinal iris

neovascularization regression. Anyway, there's a lot more work to do regarding the actual process of doing this using mass spectrometry protein sequencing that I still have to read about and add to this project.

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DETAILED UNFINISHED PROJECT DESCRIPTION

My project centers around AMD (Age-Related Macular Degeneration), a disease normally affected or caused by aging. For my project, I'll be focusing on wet- AMD, which is a type of AMD associated with abnormal CNVM (Choroidal neovascularization membranes aka new blood vessel growth) near the fundus (back inner corner of the eye which includes the fovea, retina and optic nerve, and most notably the macula) The Macula is a sensitive part of the eye that sharpens vision. When abnormal neovascularization occurs, the blood vessels that come from this can be weak and underdeveloped in the small space of the eye, causing them to break and leak harmful proteins. This damages the macula, lowering visual acuity, and eventually causing blindness. A more recently modernized form of common AMD treatment is anti-angiogenic drugs called monoclonal antibodies, predominantly created for cancer treatment but popularized for off-label use in ophthalmology. They treat cancer by inhibiting the blood vessels that feed the tumour by targeting the proteins and receptors that cause the proliferation. Without them, the tumour cannot receive proteins from the signals it sends to create proteins. This causes it to starve and shrink. In ophthalmology, mAbs have been used to inhibit the oncoming growth of blood vessels and prohibit further growth in patients with DME or w-AMD. Some of these monoclonal antibodies that I will be observing for this project are 1- Bevacizumab (Avastin). 2- Ramucirumab (Cyramza). 3- Ranibizumab (Lucentis). 4- Brolucizumab (Beovu). 5- Aflibercept (Eylea, Zaltrap) (Not a mAb, but a receptor decoy, (included in this project for comparative reasons)). Bevacizumab is a full-length antibody…. Ramucirumab is…. Ranibizumab…. Brolucizumab…. Aflibercept….

Feedback

Areas to focus on Ideas

VEGF Isoform Categorization: - highlighted the importance of VEGF isoform differences, such as the absence of exons 6a and 6b, and their impact on blood vessel characteristics. Expanding this with a more detailed comparison of each isoform’s structural properties and its angiogenic potential will

strengthen the foundation of your project. **Perhaps consider creating a visual diagram to map isoforms to their corresponding functions, particularly in the eye.**

Monoclonal Antibodies & Isoform Specificity: You're already considering drugs like Bevacizumab, Ranibizumab, and Aflibercept, each with varying affinities for different VEGF proteins (e.g., A or B). It would be helpful to explore whether specific mABs more effectively target certain isoforms and whether the clinical outcomes observed in Wet-AMD patients could be correlated with isoform prevalence in their condition.

Clinical Context and Off-Label Use: The off-label use of some cancer-related VEGF inhibitors in ophthalmology is intriguing. Comparing outcomes in off-label versus on-label usage highlights how these treatments could be optimized for Wet-AMD based on isoform presence.

Protein Sequencing & Mass Spectrometry: Your plan to utilize mass spectrometry for VEGF protein sequencing is an excellent approach to identifying and quantifying the isoforms. Since this is a complex process, it might help specify how you'll ensure accuracy and address potential challenges in distinguishing between isoforms with subtle differences in structure.

Personalized Medicine Implications: Your project emphasizes precision medicine by tailoring treatments based on VEGF isoforms. A brief section on potential applications in ophthalmology and beyond (e.g., cancer or other diseases where VEGF is key) could make your project more forward-looking.

Feedback response

1) Isoform visual diagram with corresponding vessel characteristics list in proliferation has been added to the list of items and topics on the poster board.
2) Mass spectrometry research soon determines how I will specify accuracy and potential challenges.

Title drafts

- Utilization of mass spectrometry to categorize VEGF isoforms to corresponding drugs to optimize treatment in wet AMD (Age-related macular degeneration)

- How do VEGF protein isoform development and identification through mass spectrometry impact drug variation in prognosis for Wet AMD?

My project is a research study that aims to determine whether there is a connection between the production of specific VEGF isoforms/ the VEGF proteins that proliferate as a result of that and the specialization of effective treatment (Eg- monoclonal antibodies) in wet age-related macular degeneration. Wet AMD is an ocular disease caused by weak blood vessel proliferation that breaks and leaks onto the macula of an eye, often causing vision loss. This project focuses on utilizing mass spectrometry and protein sequencing to identify isoforms and investigate the differences in characteristics between blood vessels composed of different isoforms. For example, 2 different blood vessels in 2 different patients will proliferate, both resulting in a Wet-AMD diagnosis. Blood vessels in the first patient could be composed of the isoform VEGF-121, and blood vessels in the second could be composed of VEGF-165. My project attempts to determine whether the variation between isoforms causes differences in presentation, and how mass spectrometry can optimize treatment that responds best to the isoforms found, due to the varying characteristics of blood vessels that may require different treatments to ensure success. No experiment will be conducted as this is mainly a study with some aspects of innovation regarding optimizing mass spectrometry and RNA-seq for determining isoforms and the structure, functionality and applications of a mass spectrometer in this case.
For now, the plan is to acquire and analyze preexisting mass spectrometry and protein-seq data to highlight the differences between the isoforms of VEGF and how protein structure can impact blood vessel characteristics. This can result in varying presentations and symptoms in Wet-AMD, which can allow for treatment optimization.

Section list- research

- ☑ ~~1- What is wet- age-related macular degeneration~~
- ☑ ~~2- What is VEGF and how does it impact wet-AMD?~~
- ☑ ~~2.1- VEGF-A splicing~~
- ☑ ~~2.2- The isoforms of VEGF-A~~
- ☑ ~~2.2.1-VEGF-165~~
- ☑ ~~2.2.2- VEGF-121~~
- ☑ ~~2.2.3- VEGF-206~~
- ☑ ~~2.2.4- VEGF-189~~
- ☑ ~~2.2.5-VEGF-145~~
- ☑ ~~2.2.6- VEGF-183~~

- ☑ ~~3.1- Pharmacological treatments for Wet-AMD~~
- ☑ ~~3.1- Bevacizumab (Avastin)~~
- ☑ ~~3.2- Ranibizumab (Lucentis)~~
- ☑ ~~3.3- Brolucizumab (Beovu)~~
- ☑ ~~3.4- Faricimab (Vabysmo)~~
- ☑ ~~3.5- Aflibercept (Zaltrap/Eylea)~~
- ☑ ~~3.6- Pegaptanib (Macugen)~~

Work dates: log of every day I worked on the project

Oct 15, 2024, Oct 30, 2024, Oct 31, 2024, Nov 4, 2024, Nov 5, 2024, Nov 6, 2024, Nov 7, 2024, Nov 10, 2024, Nov 11, 2024, Nov 12, 2024, Nov 13, 2024, Nov 14, 2024, Nov 15, 2024, Nov 18, 2024, Nov 19, 2024, Nov 22, 2024, Nov 23, 2024, Nov 25, 2024, Nov 26, 2024, Nov 28, 2024, Dec 1, 2024, Dec 5, 2024, Dec 6, 2024, Dec 7, 2024, Dec 8, 2024, Dec 10, 2024, Dec 14, 2024, Dec 15, 2024, Jan 2, 2025, Jan 26, 2025, Jan 26, 2025, Jan 27, 2025, Jan 30, 2025, Jan 31, 2025 (this was later continued in the other document)

This research study investigates the utilization of mass spectrometry protein sequencing and its possible applications in optimizing intraocular treatment for nAMD. It delves into how protein isoforms in blood vessels that leak onto the macula and degrade visual acuity can be biomarkers for differing presentations in nAMD. Certain isoforms can vary in characteristics due to missing parts of the genetic code, which can translate to blood vessels with differentiation. Anti-VEGF (usually administered IVT) can be altered or optimized to target isoforms with high specificity, which has shown benefits in lowering treatment burden and lowering side effects for patients. Another aspect this research project observes is the identification of anti vs pro-angiogenic isoforms and how those can be strategically inhibited through identification for optimization. This research strives to enhance understanding of the impact of biological and physiological markers in nAMD and attempts to understand how current issues within ocular research can be addressed through personalized treatment.

VEGF refs- Used refs

[1]Wet Macular Degeneration: Symptoms & Treatment
[2]Understanding Macular Degeneration - American Academy of Ophthalmology

[3]AMD REF- Exudative versus Nonexudative Age-Related Macular Degeneration: Physiopathology and Treatment Options - PMC - 3.2- use for wet AMD refs abt treatment with antiangiogenic drugs
[4]What Is the Role of Ischemia in AMD? | Retinal Physician.
[5]https://emedicine.medscape.com/article/1226030-treatment?form=fpf
[6]Comparison of Anti-VEGF Treatments for Wet AMD - American Academy of Ophthalmology
[7]VEGF-A mRNA processing, stability and translation: a paradigm for intricate regulation of gene expression at the post-transcriptional level | Nucleic Acids Research | Oxford Academic
[8]Targeting VEGF in eye neovascularization: What's new?: A comprehensive review on current therapies and oligonucleotide-based interventions under development - ScienceDirect - ref 8 opened
[9]What Is Eylea? - American Academy of Ophthalmology
[10]Zaltrap.
[11]Aflibercept in the treatment of patients with metastatic colorectal cancer: latest findings and interpretations - PMC
[12]Brolucizumab - EyeWiki
[13]The Expanding Role of Vascular Endothelial Growth Factor Inhibitors in Ophthalmology - PMC - article highlights
[14]What is mCNV? | LUCENTIS® (ranibizumab)
[15]Pegaptanib: Uses, Interactions, Mechanism of Action | DrugBank Online
[16]Pigment Epithelial Detachment - EyeWiki
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[18]Monoclonal Antibodies: Definition & How Treatment Works
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[20]Tyrosine kinase – Role and significance in Cancer - PMC. This is the reference for when you're writing about VEGF receptors.
[21]VEGFR-1 and VEGFR-2: two non-identical twins with a unique physiognomy - PMC.
[22]New prospects in the roles of the C-terminal domains of VEGF-A and their cooperation for ligand binding, cellular signalling and vessel formation - PubMed - ref 22 opened
[23]VEGF-A splice variants bind VEGFRs with differential affinities - PMC
[24]The physiological and pathological functions of VEGFR3 in cardiac and lymphatic development and related diseases
[25]Molecular Pharmacology of VEGF-A Isoforms: Binding and Signalling at VEGFR2 - PMC.
[26]Direct measurements of VEGF–VEGFR2 binding affinities reveal the coupling between ligand binding and receptor dimerization - PMC.
[27]The role of VEGF receptors in angiogenesis; complex partnerships - PMC go through thoroughly at home- ref 28 opened
[28]Vascular Endothelial Growth Factor (VEGF) and Its Receptor (VEGFR) Signaling in Angiogenesis: A Crucial Target for Anti- and Pro-Angiogenic Therapies - PMC
[29]The Carboxyl-terminal Domain(111–165) of Vascular Endothelial Growth Factor Is Critical for Its Mitogenic Potency - ScienceDirect

[30]Vascular Endothelial Growth Factor Receptor-2 and Neuropilin-1 Form a Receptor Complex That Is Responsible for the Differential Signaling Potency of VEGF165 and VEGF121 - ScienceDirect ref 30 opened
[31]Heparin-Binding Domains in Vascular Biology - PMC
[32]The vascular endothelial growth factor (VEGF) family: angiogenic factors in health and disease | Genome Biology | Full Text
[33]The pathophysiologic role of VEGF in hematologic malignancies: therapeutic implications | Blood
[34]The splice variants of vascular endothelial growth factor (VEGF) and their receptors - PubMed
[35[The heparin-binding domain confers diverse functions of VEGF-A in development and disease: a structure-function study - PubMed
[36]VEGF145, a Secreted Vascular Endothelial Growth Factor Isoform That Binds to Extracellular Matrix - ScienceDirect
[37]VEGF121b and VEGF165b are weakly angiogenic isoforms of VEGF-A | Molecular Cancer | Full Text
[38]VEGF121, a Vascular Endothelial Growth Factor (VEGF) Isoform Lacking Heparin Binding Ability, Requires Cell-surface Heparan Sulfates for Efficient Binding to the VEGF Receptors of Human Melanoma Cells* - Journal of Biological Chemistry
[39] Unique properties of 189 amino acid isoform of vascular endothelial growth factor in tumorigenesis - PubMed
[40]Angiogenesis Inhibitors - NCI.
[41]VEGF145, a secreted vascular endothelial growth factor isoform that binds to extracellular matrix - PubMed
[42]Overview of Mass Spectrometry for Protein Analysis
[43]Protein Mass Spectrometry
[44]Mass Spectrometry-Based Protein Sequencing - Creative Proteomics
[45]Protein Mass Spectrometry Made Simple - PMC
[46]Ionization Source Technology Overview | Thermo Fisher Scientific - CA
[47]Protein Structure Analysis with Mass Spectrometry | Thermo Fisher Scientific - CA
[48]Liquid Chromatography Mass Spectrometry (LC-MS) Information | Thermo Fisher Scientific - CA
[49]Triple Quadrupole Mass Spectrometer - an overview | ScienceDirect Topics
[50]Protein Mass Spectrometry Made Simple - PMC
[51]Biochemistry, Essential Amino Acids - StatPearls - NCBI Bookshelf.
52]Bevacizumab - NCI
[53]https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/monoclonal-antibodie
Ref list update from 54
[54]Monoclonal Antibody Drugs for Cancer – Caltag Medsystems
[55]Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration
[56]Pegaptanib for neovascular age-related macular degeneration

[57]vabysmo
[58]Ranibizumab for Neovascular Age-Related Macular Degeneration | New England Journal of Medicine
[59]Aflibercept summary ref
[60]Broader VEGF Pathway Inhibition for Wet AMD | Retinal Physician
[61]Laser Photocoagulation for Age-Related Macular Degeneration | Johns Hopkins Medicine
[62]Age-Related Macular Degeneration - Fighting Blindness Canada (FBC)
[63]Macular Degeneration Treatments for Dry and Wet AMD
[64]Occlusive Retinal Vasculitis Following Intravitreal Brolucizumab - PMC
[65]Side Effects of Brolucizumab - PMC
[66]What Is Avastin? - American Academy of Ophthalmology
[67]Pegaptanib (intraocular route) - Mayo Clinic
[68]Mass Spectrometry for Proteomics - PMC
[69]Protein Analysis by Shotgun/Bottom-up Proteomics - PMC
[70]Laser capture microscopy - PMC
[71]Mass Spectrometry Grade Proteases
[72]Top-down Proteomics | Thermo Fisher Scientific - CA
[73]Laser capture microdissection for protein and NanoString RNA analysis - PubMed
[74]Laser Capture Microdissection (LCM)
[75]Laser capture microdissection: Big data from small samples - PMC
[76]Levels of Protein Organization
[77]NRP2 as an Emerging Angiogenic Player; Promoting Endothelial Cell Adhesion and Migration by Regulating Recycling of α5 Integrin - PubMed
[78]Article Structure of the Full-length VEGFR-1 Extracellular Domain in Complex with VEGF-A
[79]Definition of kinase - NCI Dictionary of Cancer Terms
[80]Systemic Bevacizumab (Avastin) Therapy for Neovascular Age-Related Macular Degeneration - Ophthalmology
[81]GLOBAL PERSPECTIVES: Verteporfin Photodynamic Therapy for AMD in the Anti-VEGF Era - Retina Today
[82]VEGF Inhibition Study in Ocular Neovascularization–1 (VISION–1): Efficacy Results From Phase II/III MacugenTM (Pegaptanib Sodium) Clinical Trials | IOVS
[83]A, the structure of the VEGF splice variants. The peptides encoded by... | Download Scientific Diagram
[84]Expression of pro- and anti-angiogenic isoforms of VEGF is differentially regulated by splicing and growth factors

DATE	WORK DONE
Oct 15, 2024	Began research and accumulated references.
Oct 30, 2024,	I made a checklist of what I wanted to research.
Oct 31, 2024,	Added more references, and specified more research topics for the to-do list.
Nov 4, 2024	Accumulated more references to look at
Nov 5, 2024	Isoform tumorigenesis research
Nov, 6, 2024	I started a draft for my problem section/Introduction
Nov 11, 2024	Reference reorg day
Nov 12, 2024	Continued work on the project introduction
Nov 13, 2024	New references, to-do list editing and intro editing
Nov 14, 2024	Email draft started
Nov 15, 2024	Additional reference list to begin research/to-do list
Nov 19, 2024	Edit introduction
Nov 22, 2024	Studied the heparin sulfate interactions with proteins
Nov 23, 2024	Studied the heparin sulphate interactions with proteins, day 2
Nov 25, 2024	Teacher feedback + response
Nov 26, 2024	Title drafts
Nov 28, 2024,	Project description started
Dec 1, 2024	Rewritten priority checklist
Dec 5, 2024	Problem section draft

Dec 6, 2024	VEGF research

Dec 7, 2024	Wet-AMD research
Dec 8, 2024	Protein isoform research+mass spec research
Dec 10, 2024	Project description draft work
Dec 14, 2024	Wet AMD Research- Platform
Dec 15, 2024	Wet AMD research day 2
Jan 2, 2025	Edit checklist
Jan 26, 2025	Isoform research- platform
Jan 27, 2025	Section list made- for the CYSF platform research section
Jan 30, 2025	3- Pharmacological treatments of Wet-AMD
Jan 31, 2025	Section list reorder, VEGFR1, VEGFR2 research 2-2.1
Feb 2, 2025	Reference reorg and placement on a different doc, VEGF-A splicing research- CYSF platform
Feb 4, 2025	VEGF-A splicing section 2.1
Feb 7, 2025	NRP-1/coreceptors section
Feb 13, 2025	Exon function
Feb 14, 2025	Exon composition of isoforms and receptor diagram on render, heparan sulphate, cadherin, and integrin sections
Feb 17, 2025	Start the mass spectrometry section
Feb 19, 2025	Finish mass spec intro
Feb 24, 2025	Start drug research
Feb 29, 2025	Bevacizumab section done
March 2, 2025	Mass spec and citations list
March 3, 2025	Drug research Avastin
March 4, 2025	Complete 3 sections in the research (on the platform)
March 7, 2025	Complete the majority of the research section

March 11, 2025	Complete research section
March 12, 2025	Complete half of the mass spec section
March 14, 2025	Complete the MS section
March 15, 2025	Citations
March 17, 2025	COMPLETE PROJECT!!!!!
March 17-21, 2025	Make final edits, film presentation video, and hand in project!!!

New sections to add, maybe?

- How endothelial cell samples can be acquired from retinal tissue, put at the top of the method section
- LCMS-MS section
- Biochem intro section
- *Ocular Ischemic Syndrome - EyeWiki*. (n.d.).

  https://eyewiki.aao.org/Ocular_Ischemic_Syndrome

- discussion/conclusion section

To-do list for last week before the project is due

- ☑ ~~Bottom-up MS~~
- ☑ ~~Top-down MS~~
- ☑ ~~LCM~~
- ☑ ~~Discussion~~
- ☑ ~~Limitations~~
- ☐ Presentation
- ☑ ~~Acknowledgements~~
- ☑ ~~Finish citations~~
- ☐ Attach logbook
- ☑ ~~Abstract?~~