

Introduction to lymphatic research

Part 4

Model organisms in lymphatic research

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Molecular and Cancer Biology Research Program
University of Helsinki

October 21, 2011



Content of course lectures

- 1 The cardiovascular system vs. the lymphatic system:
Anatomy and Physiology
- 2 Molecular make-up of the lymphatic system
- 3 The lymphatic system in disease
- 4 **Model organisms in lymphatic research**
- 5 Fundamental techniques in lymphatic research
- 6 Current questions in lymphatic research



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Who is the target audience of this presentation?

- Students (2nd year and higher) of Biology or Molecular Biology that have a basic understanding of physiology (course 522043)
- All students that have started to work in our laboratory
- Anybody interested who has a basic understanding of the lymphatic system



URL

This presentation is cc-licensed and can be downloaded both as PDF and as editable .tex file from:

http://jeltsch.org/presentations_teaching

The screenshot shows a Mozilla Firefox browser window with the address bar displaying `jeltsch.org/presentations_teaching`. The page title is "Presentations & Teaching | Michael's Domain". The main content area features the heading "Michael's Domain" and the tagline "The fact that everything looks different doesn't mean that all has changed". A navigation menu includes "BLOG", "WORK", "COMPUTER", and "LEISURE". The "WORK" section is expanded to show "PRESENTATIONS & TEACHING", "PROTEINS", "PUBLICATIONS", "LISTS & FORMS", "REFERENCE", "COMPUTER", and "LEISURE". The "PRESENTATIONS & TEACHING" section is further detailed with a "2011" sub-section containing links for "Introduction to Lymphatic Research (October 2011)", "Endothelial Growth Factors in Cancer and Cardiovascular Diseases", "Lecture notes for P. Karpainen & D. Stainier", and "Academic Portfolio (January 2011)". A "2010" sub-section includes a link for "HBGS Course (May 10-14, 2010)". A search bar is visible in the top right corner of the page content.



Teaching goals

- Which animals do have a lymphatic system?
- How does the lymphatic system differ between animals?
- What animals are used in lymphatic research?
- What are the advantages and disadvantages of a specific animal model in respect to lymphatic research?



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Lecture outline

1

Intro

- Title
- Content
- Target audience
- URL
- Teaching goals
- Lecture outline
- Review of lectures 1-3

2

Model organisms in lymphatic research

- Non-vertebrates
- Do fish have lymphatics?
- Amphibians
- Reptiles
- Birds
- Mammals

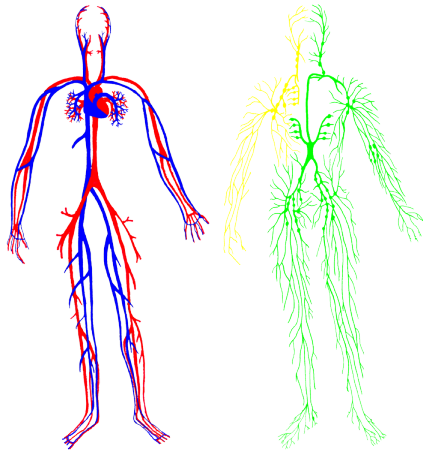
3

Outro

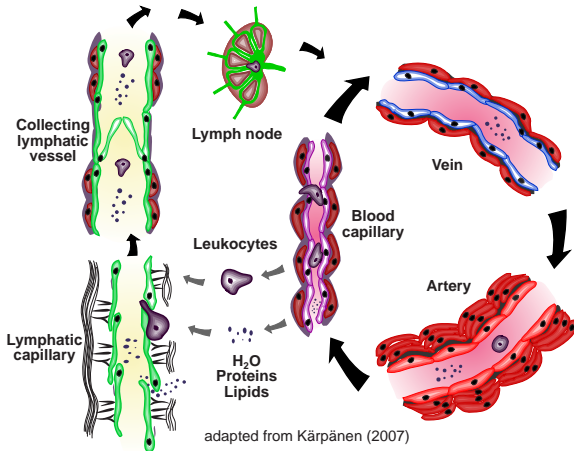
- Summary
- People
- Software



Anatomy



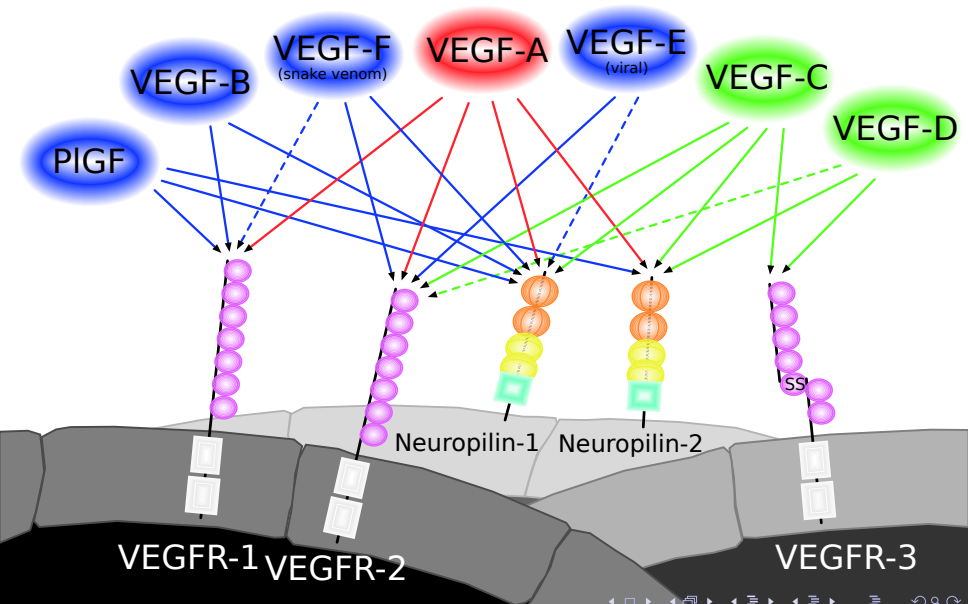
Physiology



- Drainage system to return leaked fluid into the cardiovascular circulation
- Immune surveillance by the lymph nodes
- Dietary absorption of long-chain fatty acids and other lipophilic substances

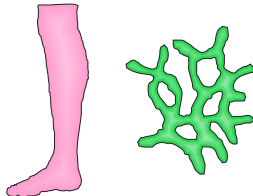


Molecular make-up of the lymphatic system

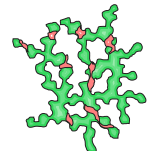
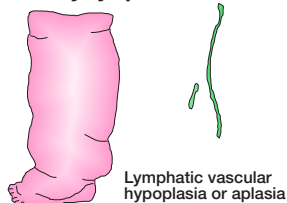


Lymphedema

Normal lymphatic vasculature

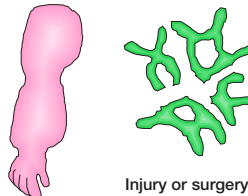


Primary Lymphedema

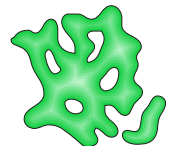


Lymphedema-distichiasis:
- Abnormal wall structure
- Lack of valves

Secondary Lymphedema



Injury or surgery

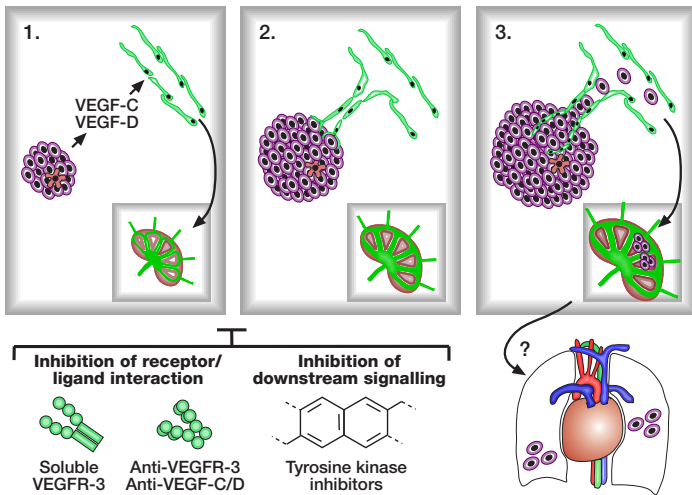


Infection

Adapted from Kärpänen (2007)



Lymphatic dissemination of tumour cells



Adapted from Kärpänen (2007)



Model organisms and animal models

Commonly used model organisms and their suitability for lymphatic research

- Mouse/Rat
- Chicken/Quail
- Xenopus
- Zebrafish
- Non-vertebrates: Drosophila, C. elegans, ...



Fruit fly, jellyfish, nematodes



Drosophila melanogaster



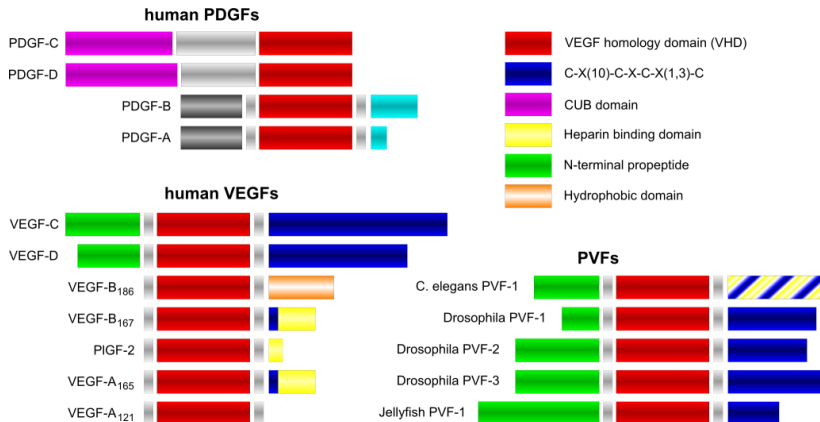
Podocoryne carnea



Caenorhabditis elegans



VEGF-C and VEGF-D are “ancient VEGFs”



Fruit fly, jellyfish, nematodes



Drosophila melanogaster
Embryonic hemocyte migration



Podocoryne carnea
Tentacle and gastrovascular tube formation



Caenorhabditis elegans
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Fruit fly, jellyfish, nematodes



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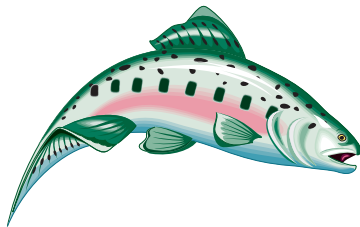
Podocoryne carnea
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Caenorhabditis elegans
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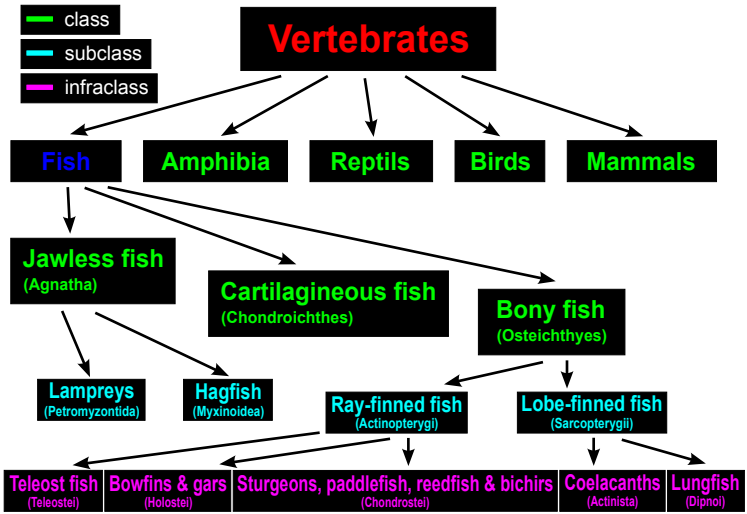
Fish



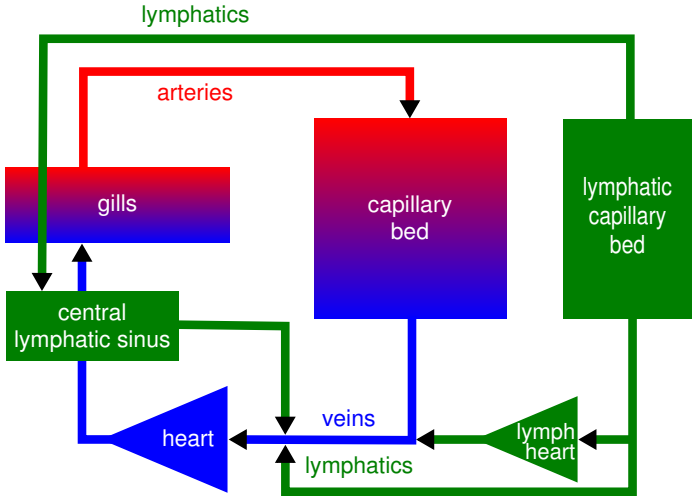
- No lymphatics in fish (Steffensen & Lomholt 1992: The Secondary Vascular System. Fish Physiology. Academic Press.)
- Kuchler et al. Curr Biol 16, 1244 and Yaniv et al. Nat Med 12, 711 describe the discovery of the fish lymphatics in 2006
- Hoyer 1938: Das Lymphgefäßsystem. In: Bronns Klassen und Ordnungen des Tierreichs 6/1: Echte Fische, Teil 2. Akademische.
- But not all fish are alike...



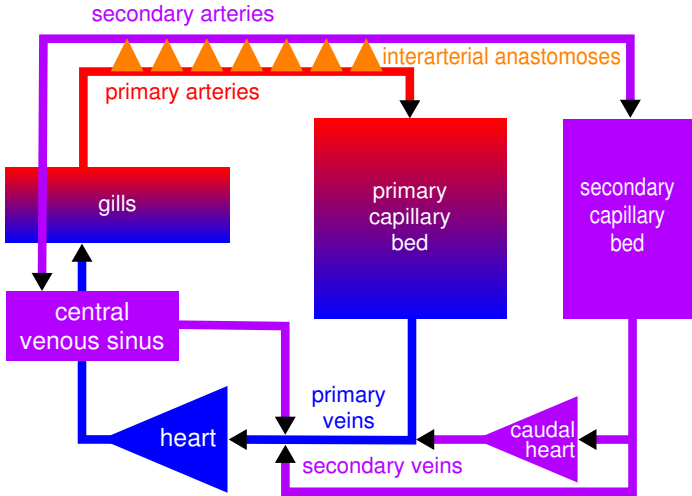
Not all fish are alike



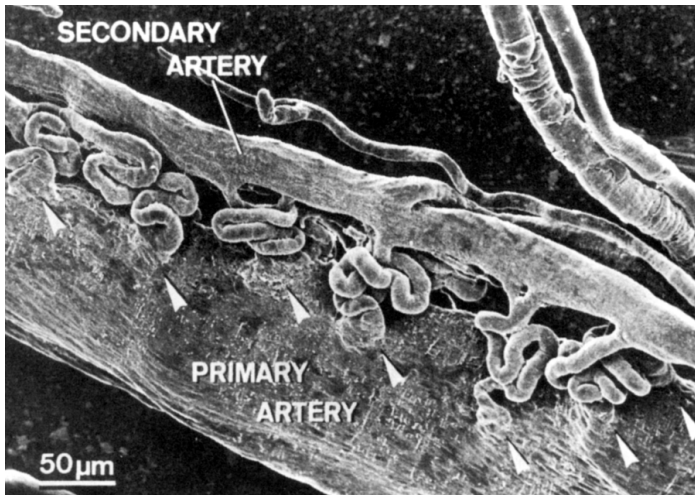
The lymphatic system of teleost fish



The secondary circulatory system of teleost fish



Arterioarterial anastomoses



Vogel (1985)

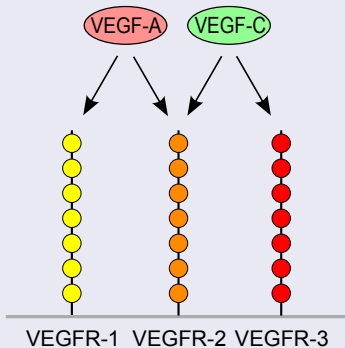


Many open questions

- The piscine secondary circulatory system: a re-labeling of the lymphatic system?
- Arterioarterial anastomoses: A modification of the lymphatic system in some fish to increase flowrate or a casting artifact?
- Molecular correlates of anatomy?



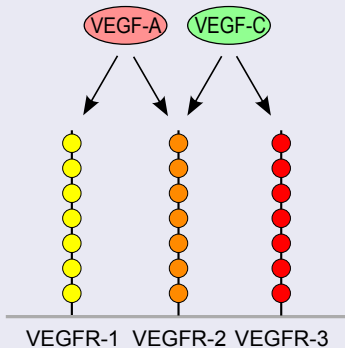
Homo sapiens



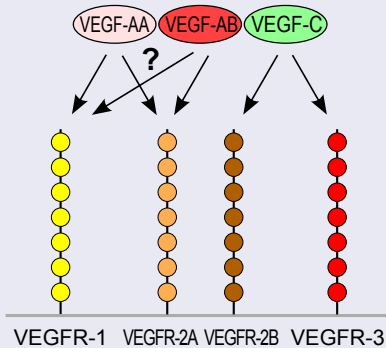
Danio rerio



Homo sapiens



Danio rerio



Amphibians



- Lymphatics function in fluid homeostasis
- Dermal lymph sacs in frogs and toads
- 50x more lymph formed compared to humans
- Many lymphatico-venous communications with lymph hearts



Reptiles



- Reduction of lymph hearts & lymphatico-venous anastomoses
- VEGF-F in snakes



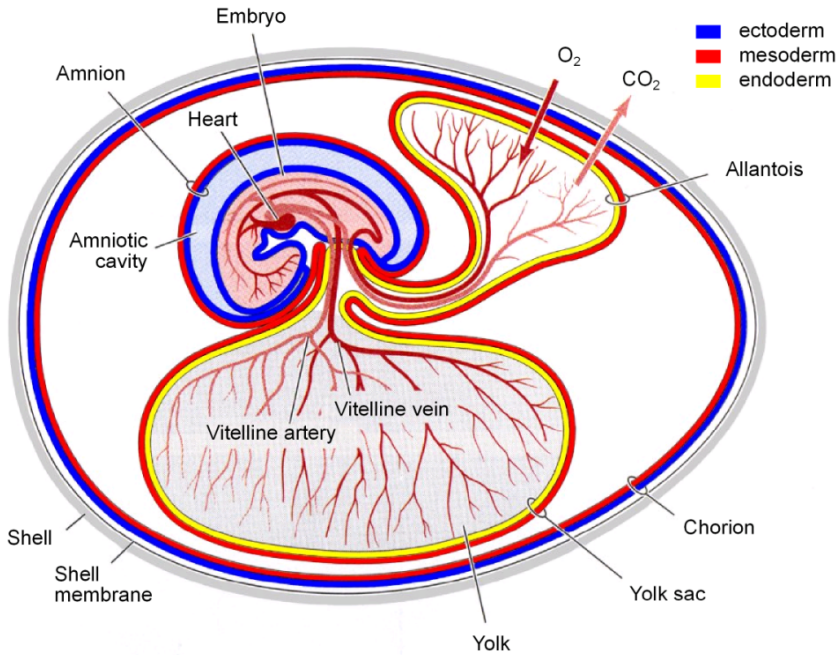
Birds



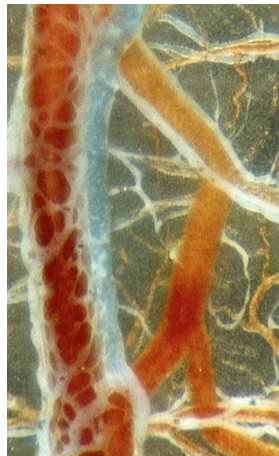
Photo by Fir0002/Flagstaffotos

- Lymph hearts disappear
- Lymph nodes appear in aquatic birds
- The chorio-allantoic membrane is rich in lymphatics





The CAM vasculature

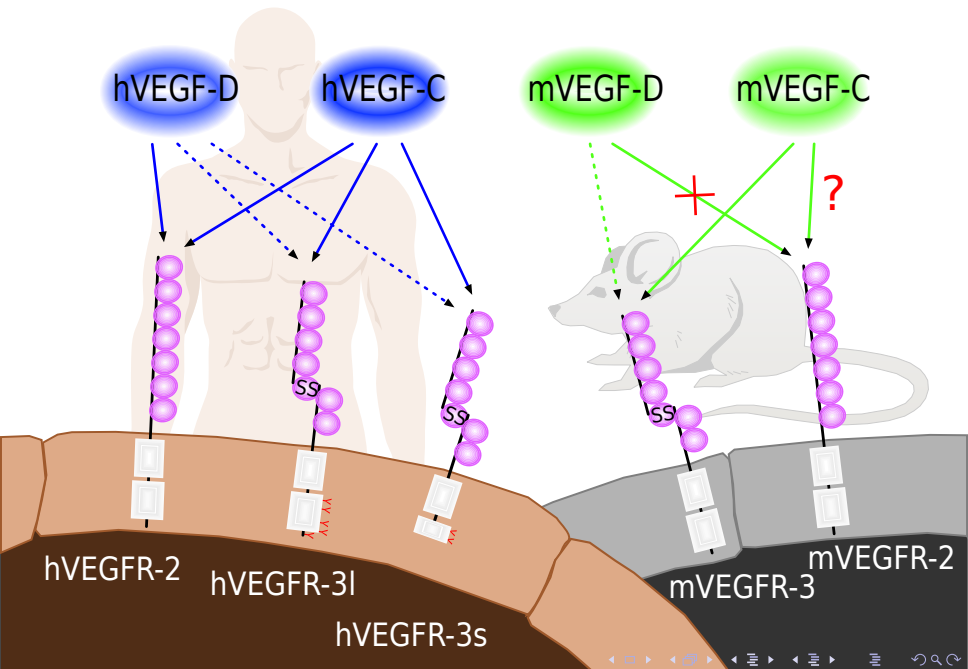


Why mice are not men



- Difference in hydrostatic pressure has implications for lymphedema models
- Significant differences in the molecular make-up of the VEGFR-3 signalling system





Summary

- Non-vertebrate organisms have no lymphatic system, but they have homologous molecules
- Central questions about fish lymphatic anatomy and physiology are unanswered
- The most frequently used animal model for lymphatic disease is the mouse despite limitations due to size and molecular differences to humans





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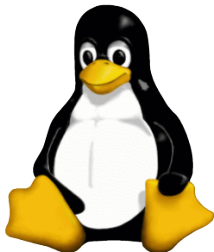
- Kari Alitalo
- and the rest of Molecular/Cancer Biology Laboratory

UNIVERSITY OF GÖTTINGEN

- Jörg Wilting



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