Digital Embryology Consortium

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Digital Embryology Consortium

Mission

To preserve, protect and share the historic embryology collections of the world.

Background

There are only a few large collections of human embryological material currently existing worldwide. These collections are held in universities and associated research institutions as either whole fixed embryos or more commonly sectioned and histological stained slide material. Many of these collections are between 30 to 100+ years old, and can be classified as historic.

Much of the histological material is sections on large format slides and even with optimal storage and with careful use, they have begun to deteriorate and will eventually be lost.

To address this issue a discussion was held with collection curators concerning the establishment of a scientific research partnership of collections: the Digital Embryology Consortium (DEC).

The purpose of this research consortium is to digitally scan each embryo slide collection as it currently exists. This process will:

1. **Preserve** – Digital slide scanning will establish a permanent electronic copy of each histological section as it currently exists, preserving the material against future degradation of both the fixed biological material and histological stains.
2. **Protect** – Digital slide scanning will minimize the future handling of the original irreplaceable histological slides that have been damaged in the past by their environment, researchers and transport.
3. **Share** – Digital slide scanning will establish an online database of histology slides for research and educational use. In the past individuals had to travel to each embryo collection, which could only accommodate limited research access to each collection.

There have been previous attempts to partially document some of these collections, but the equipment and technology was not sufficiently developed to allow the process to be complete and in some cases the data was restricted in availability. The Kyoto collection had already commenced digitization of their histology collection, as well as imaging their whole embryo material. The Carnegie collection had also previously had some slides scanned. The curators were supportive of this consortium proposal, but unable to raise or allocate the funds to carry out this project program.

Project Proposal

Since 1997 I have provided an open online embryology research and education website that has involved collaboration with many researchers and institutions. Based upon this and other work I have published embryology papers, chapters and books. The work has also received international recognition, national and university teaching awards. Today this website exists as the most popular online embryology education resource.

In 2007 I received a personal research endowment that had two stipulations: firstly, that the money be used for equipment; secondly, that the research has a fieldwork component.

In 2013 I visited on study leave many of the major collections (Kyoto, Berlin, Blechschmidt, Madrid) as well as communicating with the curators of other collections (Washington, Vancouver). During the period I was able to access, study and photograph material within these major collections.

In 2014 as a partner in the consortium, the 2007 research funds have now been applied to the purchase of microscopy equipment, support hardware and services that will allow digitization, storage and online access to these collections for the consortium.

In 2015 this equipment, with the support of the scanner supplier Zeiss, will be delivered to each of the embryo collections. The scanner will initially be located at one of the European collections and once the collection had been digitized, relocated to the each collection in turn to eventually scan all collections. Zeiss recognizing the importance of this project has offered to assist with the delivery, installation and training at each of the collection sites. Equipment transport/storage cases have also been purchased to aid this process. Note that while the consortium is a non-commercial project, we also recognize the valuable assistance of Zeiss in supporting the project aims. Once the embryology digitization project has been completed the scanning equipment will be relocated to the School of Medical Sciences, UNSW Australia for future research use.

My project partner role will be to coordinate the project, communicate with consortium partners, be involved with transport and establishment at each site for scanning, establish the online website and database. Also, along with consortium partners, to raise additional research funds to support both the project and consortium.

Consortium partners will be involved in all aspects of this project. When the scanner is located at their collection, their role will be to identify “in-house” resources and staff to assist with the scanning process. Each partner will also act as the site contact for equipment training, service and repair. Currently there are funds also available for minor equipment repairs, transport and insurance. Each consortium partner will receive upon scanning completion, a digital copy of their own collection for their own use and electronic preservation of the collection.

A key partner contribution future component to the project will be to make available online in the contributor's own language the collection background information, documentation and supporting text. All content will also be made available where possible in English.

The notes below provides for consortium partners background information on the scanner equipment and software selection for the project. Note that there are additional human embryo collections that may in the future also contribute to the consortium.

Equipment

The key piece of equipment to this project will be the purchase of an appropriate digital slide scanner. Minor requirements were bar coder, hard drive duplication devices and hard drive storage for the digital images.

1. Slide Scanner

Four main suppliers of digital slide scanners were initially identified: Leica (Aperio), Coherence, Olympus and Zeiss. Each scanner was analyzed using criteria required for this project before final equipment selection. A general summary for each criteria is shown below including the selected scanner information.

- **Handling** - To minimize slide handling during scanning. Some of the scanners required loading of individual slides into trays where each slide was then mechanically handled from the tray and then re-transported individually by the scanner. This process would expose slides to possible handling and transport damage. The Zeiss Axioscan Z1 slides are loaded onto a tray system, and only the tray handled by the scanner.
- **Slide format** - To handle the large historic slide format (2 x 3") as well as the smaller modern slide format. Some of the scanners only handle the modern slide format, or allow only single slide loading of larger format slides. The Zeiss Axioscan Z1 **s**lide trays formats are available for both the older large slides and the modern smaller slide format.
- **Slide resolution** – To scan at a high resolution, approximately x20 objective optical resolution. All scanners were able to meet this criteria.
- **Slide throughput** – To scan at a high resolution, approximately x20 objective optical resolution. Some of the scanners had tray systems for loading slides in number, some only allowed single slide loading of different (larger) format slides. The Zeiss Axioscan Z1 tray system allow automatic scanning of up to 50 of the large slide format. Trays can also be "hot swapped" during scanning to replace already scanned trays, increasing slide throughput.
- **Digital image format** – To store images in a format readable by a range of software. Some of the scanners use proprietary image formats stored in commercial database software and readable only by supplied software or applications. The Zeiss Axioscan Z1 image format (CZI file) can be read by proprietary software (Zen) supplied with the scanner and browsed on a number of different platforms. The image format is also readable by the non-proprietary software proposed for this current project.
- **Transport** – To be transportable to different geographic sites. All scanners were designed to be installed as a single location, they and varied in their potential and practicality to be transported between sites. The Zeiss Axioscan Z1 was compact and has transport cases available and support for the process was an advantage.

2. Bar Coder

If required, individual slides can be barcoded prior to scanning and an off-line database established for coordinating scanned slides with original collection annotations. Note the scanner provides a unique slide ID and an overview image (low resolution) of each slide. Metadata can also be added to slide images during processing or after scanning.

3. Hard Drive Storage

Digital images will be archived on external storage and additional replica copies made available to the original collection curators. A drive duplicator with removable hard drives will be provided and transported with the scanner. The file size of each scanned section will vary depending on section size and scanning resolution. At the proposed scanning resolution each scanned slide file size would range from 100 Mb to 1.5 Gb. (e.g. Blechschmidt approx. 9000 slides at 1.5 Gb the total is about 13 Tb). The total DEC project will be in the order of 60+ Tb of image files. A spreadsheet will be completed in parallel with the scanning process to provide coordination with scanner image ID and additional embryo and slide annotations. This will be a reference resource for each collection and form the initial basis of an online information database.

Management of Digital Images

In order to support the collaborative nature of this project, the image database will reside at an address that is not specifically affiliated with any one institution. For this specific purpose I have purchased the web address (http://human-embryology.org). Note that in addition to online collection availability, each institute would be provided with a hard drive copy of their own collection material to be used as they choose. The consortium copy will also if required act and be available as an archival or full backup of the institutional copy.

1. Digital Image Software

There are two main options for the storage, analysis and sharing of the scanned digital images:

1. The supplied commercial Zeiss Zen image software allows easy image storage and analysis on the associated computer. Online distribution requires purchase of storage space.
2. The Open Microscopy Environment (OME) open-source software and data format standard specifically designed for the storage and manipulation of biological microscopy data. This free software allows the online distribution and analysis of digital images suitable for this project.

The commercial cost of purchasing storage for online sharing of images using Zen software would be prohibitive for the size of this project. The OME option will be significantly more flexible and has the good scientific community support.

2. Digital Image Database

The physical location of the online database server is currently being determined. The Open Microscopy Environment (OME) freely provides OMERO software that can act as a secure central repository. OME online information states that images can be viewed, organized, analyzed, and shared from anywhere with internet access. The images can be analyzed from a desktop application (Windows, Mac or Linux), from the web or from 3rd party software. Over 130 image file formats are supported, including Zeiss (CZI format) and all

other major microscope formats. This will allow images provided from other collections and scanners to be incorporated into the existing consortium database. There is also client side software that allows the batch uploading of images from a variety of geographic locations.

The website will include additional resources for consortium partners including collection background information, curator image annotations, and a Wiki discussion area for both database partners and registered users. A key component of this support information will be its availability in the languages of the original collection sources.

3. Digital Image Reuse

It is proposed that each institute will continue to hold and control the rights to their own collection materials. Each institution will be provided with a hard drive copy of their material to be used as they choose. The Digital Embryology Consortium will make the scanned images freely available to online registered users at a specific address (http://human-embryology.org) for research and educational use. The database organization and metadata will maintain the identity of each collection and not "rebadge" any content. There will no charge for online user registration or image access, and a database will be maintained of all registered users for information and contact purposes.

Registered researchers or educators intending to publish either images or analysis derived from collection images will be required to obtain permission as currently required by each collection when using the original slides. This condition will be a requirement of registration for online access to the consortium images, as well as provided in the online information. Note that the consortium covers many different institutions with different requirements for reuse. Institutions can only supply permissions for their collection images under their own institutional conditions including copyright, publication co-authorship, or acknowledgement. Authors using multiple collections would need to contact each institute for permission.

Alternatively, the Digital Embryology Consortium could in future with institutional approval, develop its own global policy for reuse permissions. This option does not form part of the current consortium proposal.

The Digital Embryology Consortium only requires acknowledgement, including the internet address, for providing access to the digital images. As a courtesy, authors can also supply the consortium information about specific publications or image reuse.

With the permission of institutes, and available to users without registration, a small number of collection images will be accessible on the consortium website for general information and user tutorial purposes.

Project Timeline

- Jul 2013 to Jan 2014 - Visit or contact human embryology collection curators with digital consortium proposal.
- Jul 2014 to Oct 2014 – Informal confirmation of consortium and its agenda. Equipment and software assessment, contact with suppliers and user groups.
- Nov 2014 – Tender equipment quotation and logistics.
- Dec 2014 – UNSW Institutional approval for equipment purchase.
- Feb 2014 – Distribution of mission, agenda and timeline for partner institution feedback.
- Mar 2015 – Meeting with collection institutions to finalize consortium agreements and sequence of scanning.

- Apr 2015 – Equipment Gottingen delivery to commence Blechschmidt collection digitization. Initial images used for test database.
- May 2015 – Review of scanned materials and establish test database.
- Apr 2015 to Dec 2015 – Scanning of European collections (budgeted approximately 3 to 4 months to scan each) and require equipment shipping between collections.
- Dec 2015 – Shipping to USA.
- Dec 2015 to Jan 2016 – Commence scanning of the Carnegie collection (budgeted 8+ months to scan). Will include scanning of Vancouver collection.
- Dec 2016 – Shipping scanner to Australia.

Note that final equipment return shipping date is flexible and entirely dependent upon collection scanning being completed along this draft timeline and also whether additional collections choose to participate in the digitization project using the supplied scanner.

Concluding Remarks

This research consortium is a unique opportunity. Where the latest scanning and online technologies have now developed to the stage that we can make available to the scientific community these historic human embryology collections. Over the years collection slides have been lost, misplaced, damaged or their histology stains degenerated never to be seen again. Scanning will preserve these collections as they now stand against future losses. These collections had been prepared and studied by pre-eminent embryologists, establishing key concepts in our understanding of human development. Few later researchers could easily access and study the collections. With partner institution collaboration, these embryo collections are now ready to be shared and explored again using new technologies and new embryologists eyes.

Collections

1. Blechschmidt Collection - University of Goettingen, Germany Prof. Christoph Viebahn (Head of Embryology Department).
2. Embryological Collection - Museum für Naturkunde, Leibniz Institute for Research on Evolution and Biodiversity. Dr Peter Giere (curator of the embryological collection).
3. Madrid Collection - Complutense University of Madrid, Institute of Embryology. Prof. José F. Rodríguez-Vázquez (Head, Embryology Institute of Complutense University of Madrid).
4. Carnegie Collection – National Museum of Health and Medicine Elizabeth Lockett (curator NMHM).
5. Kyoto Collection - Congenital Anomaly Research Center, Kyoto University Graduate School of Medicine, Kyoto. Prof Shigehito Yamada (curator of the embryo collection).
6. Perry-Arey-Milligan Collection - University of British Columbia, Prof Virginia Diewert (Professor of Orthodontics). Unconfirmed contributor

Online Resources

1. Digital Embryology Consortium
   http://human-embryology.org
2. Human Embryology Collections
   https://embryology.med.unsw.edu.au/embryology/index.php/Human_Embryo_Collections
3. Zeiss Axioscan Z1
   http://www.zeiss.com.au/microscopy/en_au/products/imaging-systems/axio-scan-z1.html
4. Open Microscopy Environment
   https://www.openmicroscopy.org/site