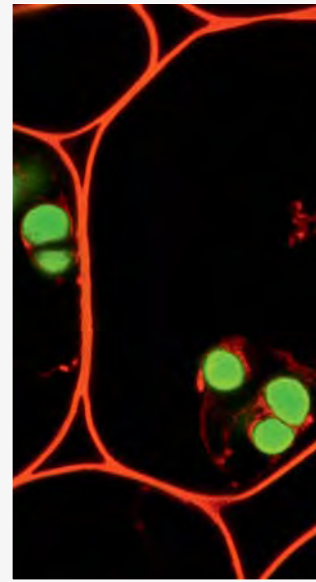
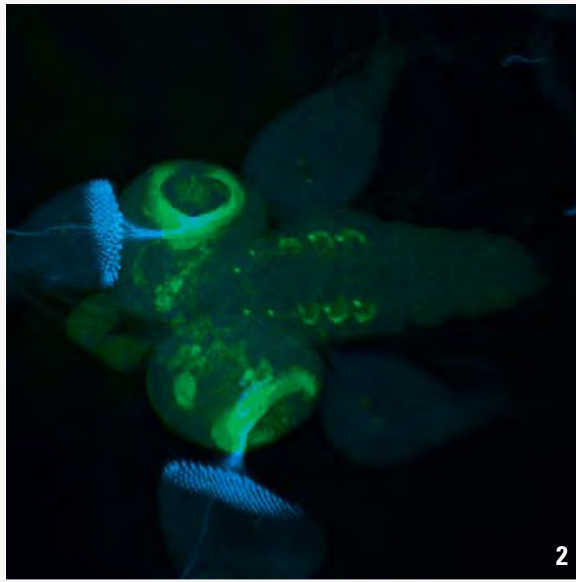


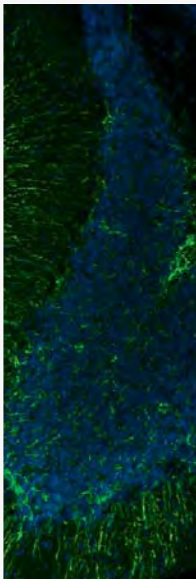
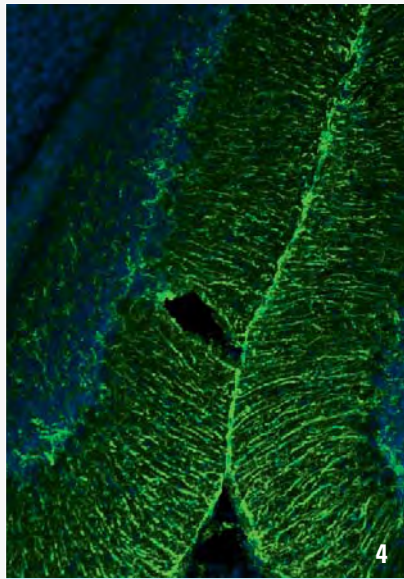
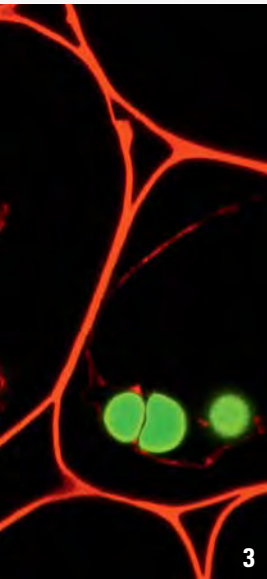
Leica TCS LSI

The World's First Super Zoom Confocal!
From Gene to Cell - from Cell to Embryo



- The World's First Super Zoom Confocal
- *In Vivo* - Large Scale Imaging
- Freedom for New Reserach
- Easy to Achieve





An increasing number of scientists extend their focus of bio-research from single cell studies to entire organisms, analyzing the complex interaction within whole animals. Thus, modern developmental biology is an emerging field of research, studying the dynamics of cell growth, differentiation processes and the development of organs *in vivo*.

As living organisms grow in three dimensions these studies require imaging systems which provide - beside high resolution – a large workspace and field of view. Leica Microsystems introduces a pioneering imaging system for developmental biology which provides all these features in one: the new Leica TCS LSI.

Leica TCS LSI

The world's first super zoom confocal!

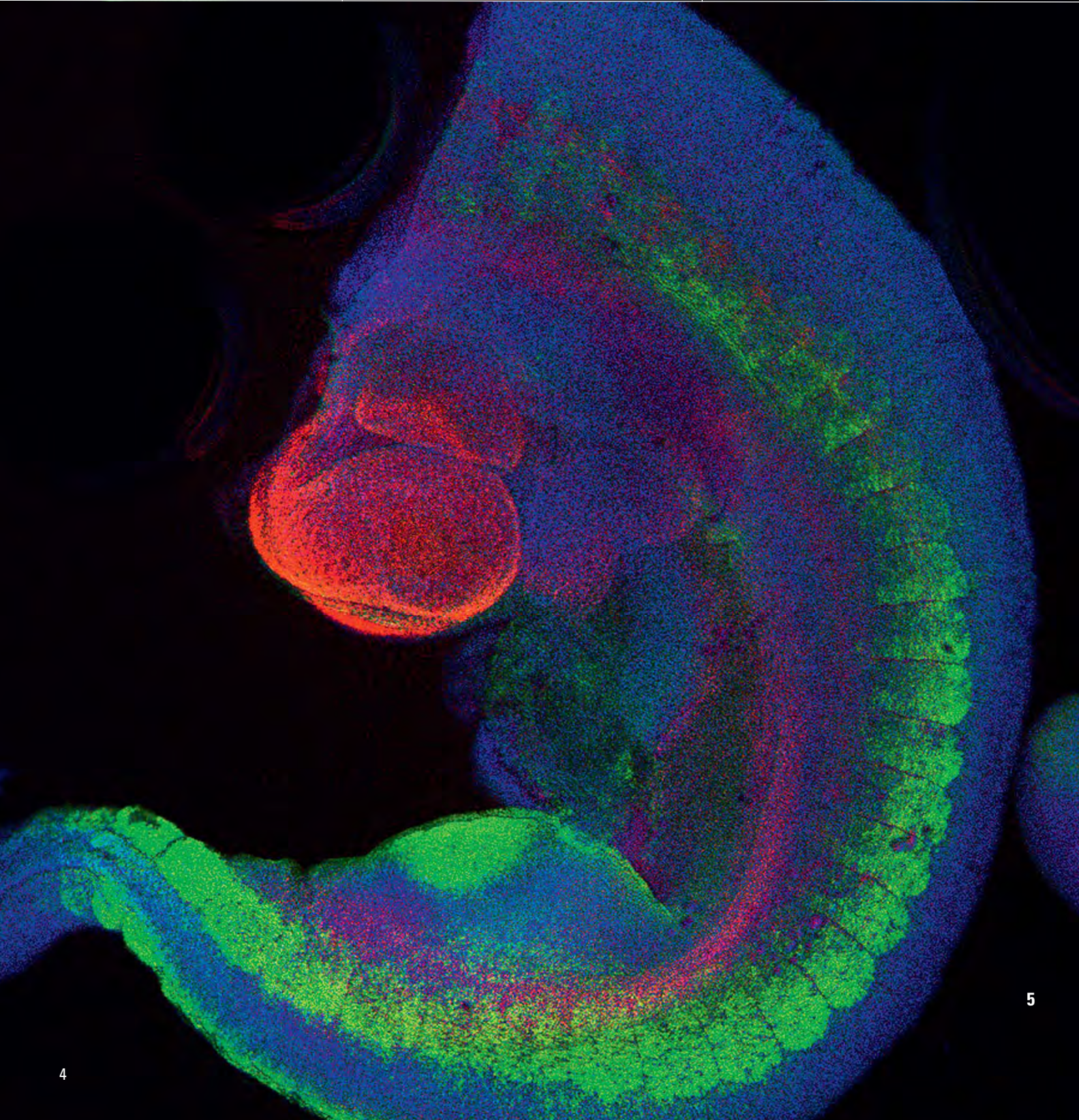
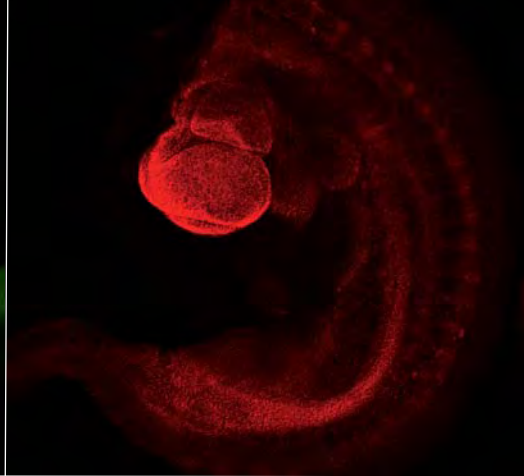
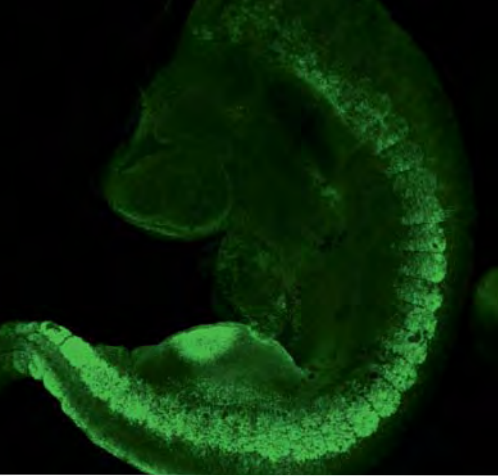
Leica TCS LSI is the first super zoom 3D-confocal, offering high resolution plus large field of view for *in vivo* imaging. The new Large Scale Imaging (LSI) platform provides generous workspace and adapts perfectly to the experiment needs of native specimen analysis.

True confocal technology is used to provide crystal clear images of highest spectral resolution, revealing finest details of the model organism, no matter if drosophila fly, mouse, plant or zebra fish.

An automated optical zoom system allows for seamless magnification change on demand, easy switching from overview to details and free 3D navigation through the specimen.

Gain new insights with *in vivo* imaging by Leica TCS LSI and study processes of life – from egg to fly, from embryo to adult.





Benefit from freedom for new applications offered by Leica TCS LSI, feel free to zoom in and out and travel time resolved in all dimensions *in vivo* through your specimen.

Leica TCS LSI

New perspectives of life: From cell to animal

A system tailored to your needs

With the Leica TCS LSI, study the process of life from embryo to adult. Due to the functional and workflow oriented design, even sample preparation and orientation can be directly performed on the imaging system.

Take advantage of the combination of high-resolution confocal technology and large field macro zoom imaging. A generous workspace provides extended freedom for *in vivo* experiments. Zoom in and out, from overview to area of interest at highest resolution and obtain fascinating results.

From cell to embryo

Leica TCS LSI enables you to visualize cell growth and the fascinating differentiation of cells into organs in real life from cell to embryo – in one system!

Identify new pathways from gene to cell, from cell to animal; or examine the influence of genomic defects on the whole animal. Study time resolved 4D processes at highest resolution easily as Advanced Time Lapse software is provided for *in vivo* studies.

Analyze protein interactions or test the influence of drugs *in vivo* in bio-medical research.

Visualize the development of life: the Leica TCS LSI Large Scale Imaging System provides highest image quality, easy operation and maximum flexibility.

Features

- Zoom factor up to 16x
- Field of view up to 16 mm
- Generous workspace
- Free sample access by wing door
- Easy sample manipulation
- Largest motorized z-control
- Large xy-travel range for optimal positioning
- Precise z-control by galvo stage



Largest workspace...



...for finest insights

Leica TCS LSI – The Large

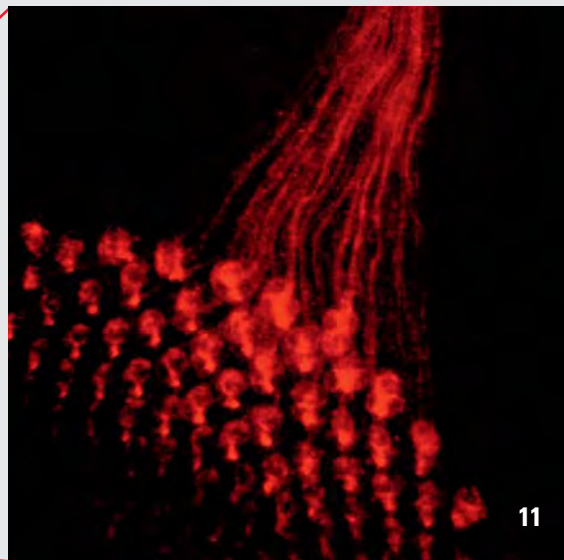
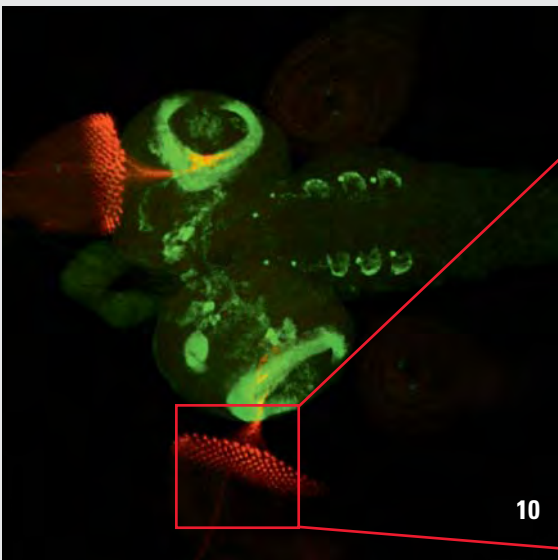
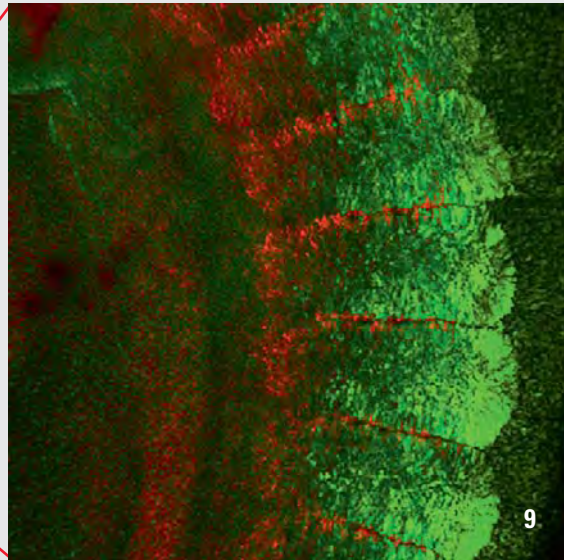
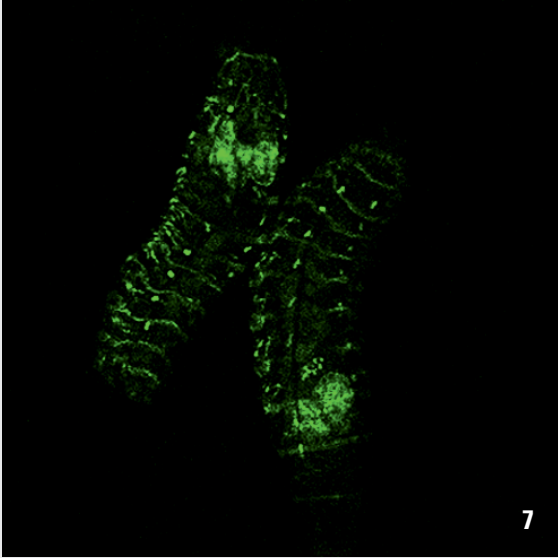
High Resolution in 2D and 3D

From micro to macro ...

Get the big picture of large specimen in 2D or 3D. Use the Leica LAS AF 3D-visualisation package for reconstruction of *Drosophila* larvae. (Left)

... zoom in seamlessly into the finest details!

The motorized optical zoom offers the advantage of flexible magnification to identify the finest details of your model organism. Backbone details of zebra fish or eye of the *Drosophila* larvae, both in highest resolution. (Bottom)



Scale Imaging *In Vivo* Confocal

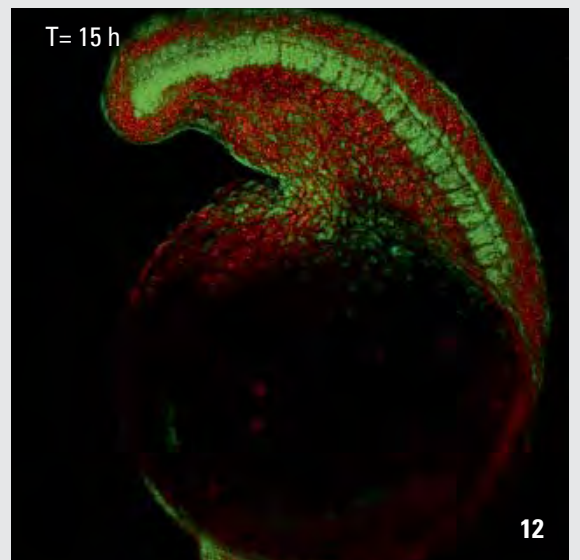
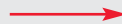
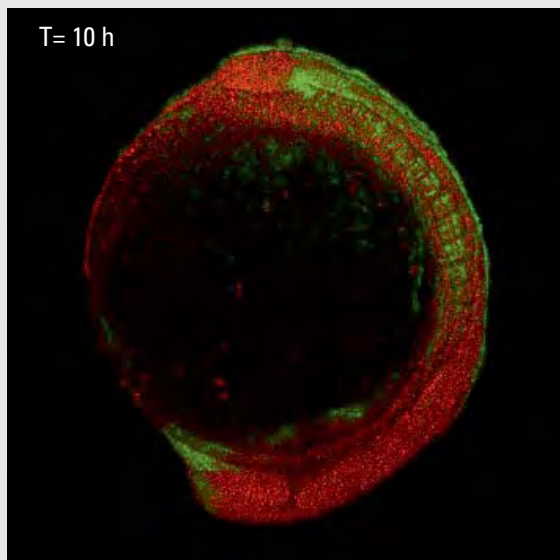
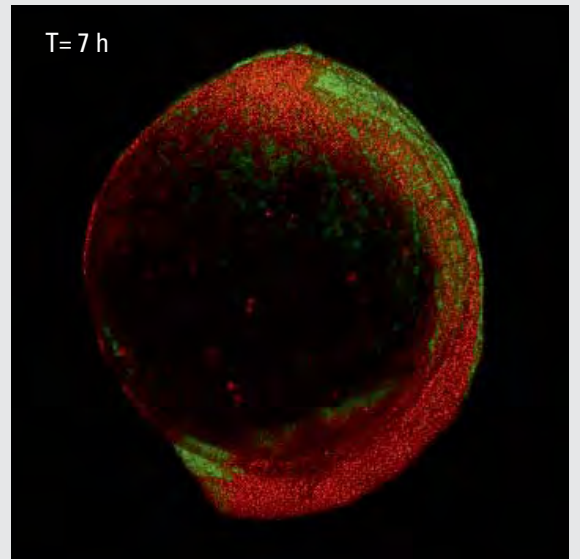
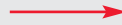
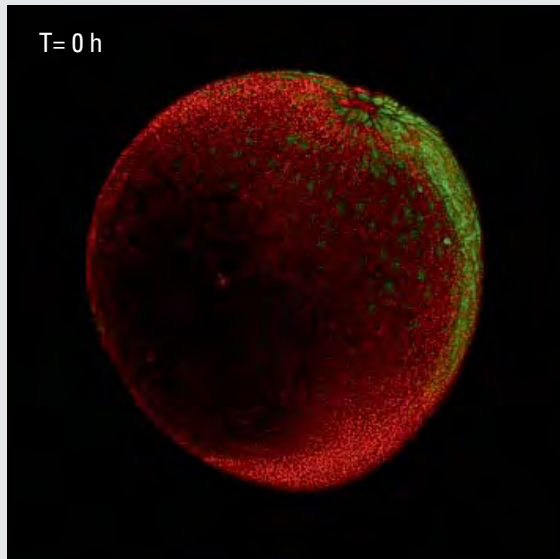
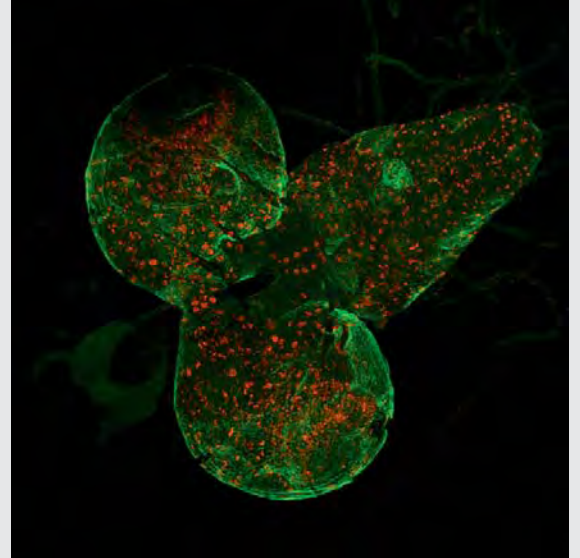
4D-Advanced Time Tapse

From larvae to fly ...

Tracking the development of life over time offers exciting insights for embryology and morphogenesis – all in the same specimen! (Right)

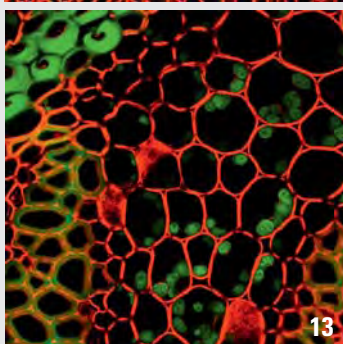
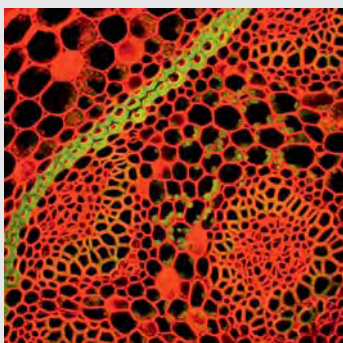
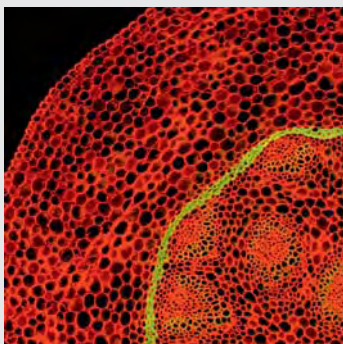
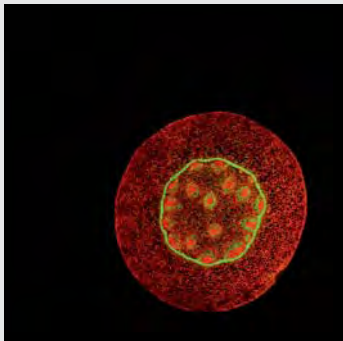
... from egg to fish, achieve excellent results in 4D!

To obtain exciting views of the development of organs with LAS AF Live Data Mode software and see the backbone formation during the growth of a zebra fish. (Bottom)



Dynamic studies *in vivo*

- 2D, 3D and 4D analysis
- Advanced Time Lapse
- Spectral analysis
- Photo activation with 405 nm
- Micromanipulation



13

Seamless zooming in and out

More freedom than ever: For various specimen sizes and research questions, micro- and macro objectives can be used. High resolution and largest field of view enable a wide range of new applications. For excellent new research opportunities the Leica TCS LSI offers variable magnification with a field of view up to 16 mm plus large and precise z-positioning – all in one system.

In Vivo – Large Scale Imaging

High resolution from micro to macro

A comfortable start

Instead of engineering the living object through holes into incubators, start to place your specimen easy and securely through wide-open wing doors of the laser safety chamber. Gain overview first by digital camera for easy orientation. Fine-focus precisely either with the tuning wheel of Universal Microscope Control or by LAS AF software.

Study the changes of life in 3D

With Leica TCS LSI, you navigate through your model organism from large to small and back, identifying functions and obtaining insights never seen before. From the entire animal up to the finest detail the motorized zoom offers the advantage to select any area of interest – without changing the objective! Fine-tune the z-position through the highly precise SuperZ Galvo stage and orientate the sample perfectly in xy-direction with a high precision motorized stage.

Ultra dynamic z-control

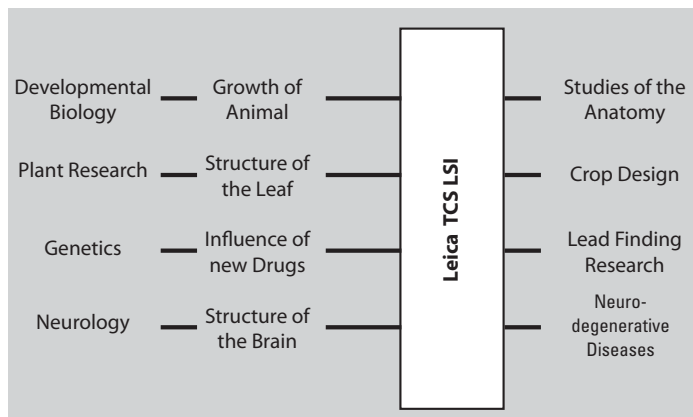
The flexibility of the Leica TCS LSI is unique in confocal microscopy. The SuperZ Galvo stage offers backlash free sensitive vertical positioning with a maximum travel range of 1500 μm . The fine focus integrated in the motorized zoom system allows further to extend the focus range by 10 mm. Finally, ultimate z-position control is achieved by the motor focus itself, travelling up to 150 mm.

Free xy-sample positioning

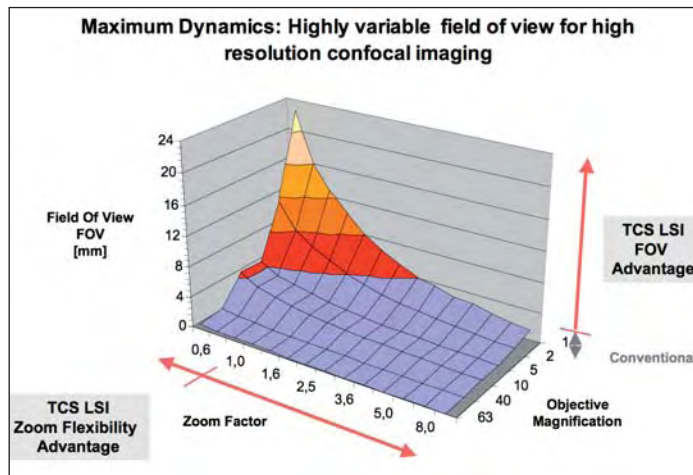
Leica TCS LSI systems provide a maximum travel range, independent of the type of stage. Both, manual and automated stages offer a wide range for ideal sample positioning.

Increased cell-viability and highest resolution

Obtain brilliant fluorescent images over long time. Ultimate image quality is provided by true confocal point scanning technology. The Leica TCS LSI offers a variety of automated tools to adjust excitation and emission perfectly to your individual sample conditions. Maximize signal efficiency with the freely tunable spectral detector, the highly dynamic photomultiplier and minimize laser excitation power with the 100%-tuneable AOTF-attenuation. This maximizes the lifetime of your specimen.



Examples of Leica TCS LSI applications



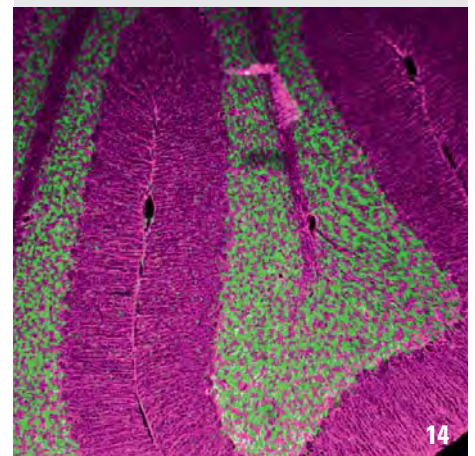
Field of view depending on objective and zoom adjustment

Research areas

- Developmental biology
- Embryology studies
- Morphogenesis
- Embryo genetics
- Plant science
- Genetics
- Proteomics
- Neurology

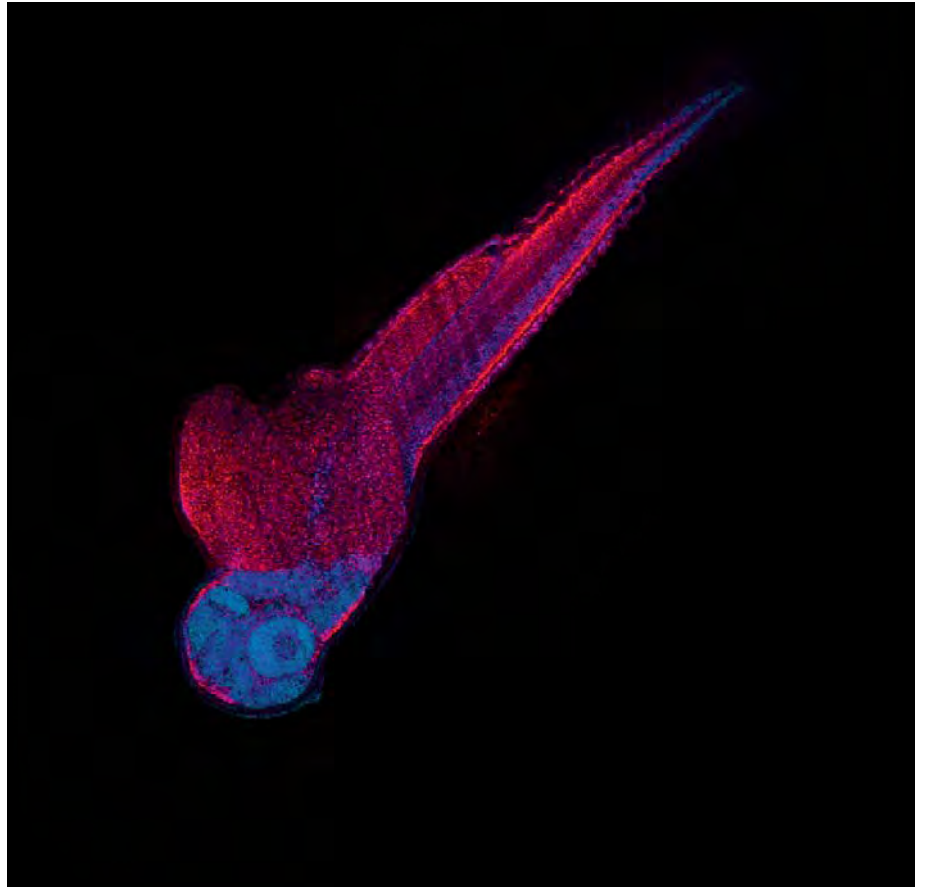
Applications

- Cancer research
- Agriculture investigations
- Pharmaco screening
- Seed development
- Cell development
- Heart diseases
- Brain development



New Dimensions

- Generous workspace
- Free sample access by wing doors
- Easy sample manipulation
- Largest motorized z-control
- Hardware for most flexible use
- Large xy-travel range for optimal positioning
- Precise z-control by galvo stage
- Motorized and manual xy-stages
- Accessories for environmental control of temperature, CO₂, humidity



Making life visible in 4D

Even more than the static view, it is fascinating to observe the development of whole organisms over time. The Leica TCS LSI with LAS AF Live Data Mode Software offers perfect automation for cell development studies, from egg to embryo. Individual experiments can be easily combined to a fully automated workflow. The door is open for continuous studies from cell to adult.

Advanced Time Lapse

High resolution from cell to embryo

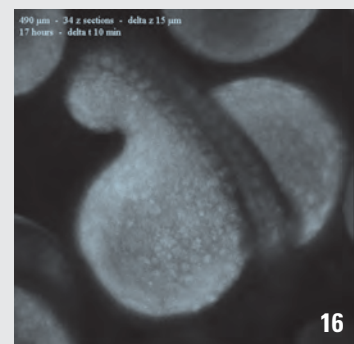
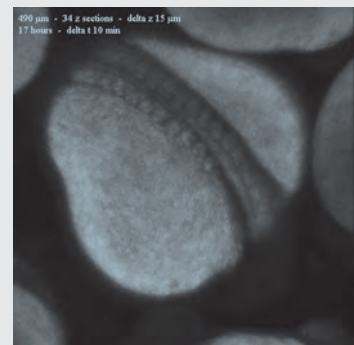
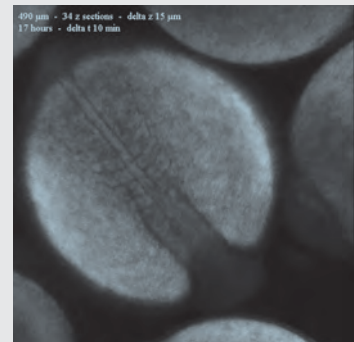
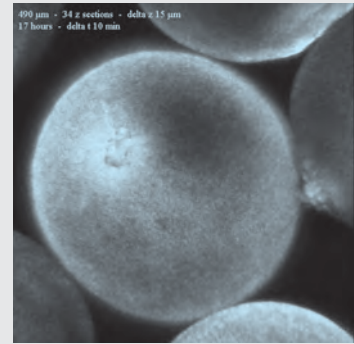
Perfect climate included

Optimal growth conditions for living animals can be provided by a wide range of accessories. The laser safety cabinet is converted into a climate chamber just by adopting a heating unit for precise temperature control. Stage adapters for CO₂-gas and humidification offer optimal sample conditions. Even during the experiment, remote controlled manipulators enable active specimen handling within the native environment.

All accessories are offered in modular and approved kits for easy system upgrade on demand, ready for today's and future experiments.

Following the changes of life

Studying movements of cancer cells in bio-medical research, investigating translocations after photo-activation, studying the growth of bio films on large implants: The creativity for future experiments will come from you, the extended freedom for new research applications is provided by Leica TCS LSI.



Zebra fish development video

Confocal technology

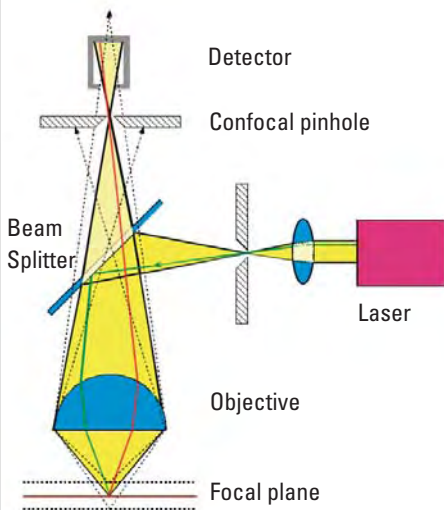
- Highest resolution
- True confocal point scanner
- Spectral detector
- Solid state laser
- 405, 488, 532, 635 nm excitation
- AOTF controlled
- Fully automated
- Easy to use

Crystal clear 3D images – The benefits of true spectral confocal imaging

Leica TCS LSI is equipped with a true spectral confocal scanner that provides ultimate crisp resolution. Scanning the specimen in thin optical layers and detecting the fluorescence signal point-by-point results in images free from the stray light of adjacent elements. The result – brilliant images at very high resolution.

The World's First Super Zoom Confocal Technique for new perspectives

The Confocal Principle

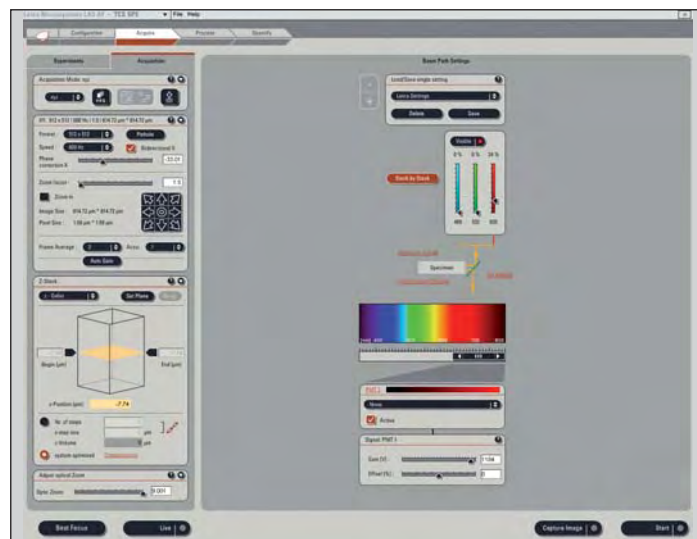
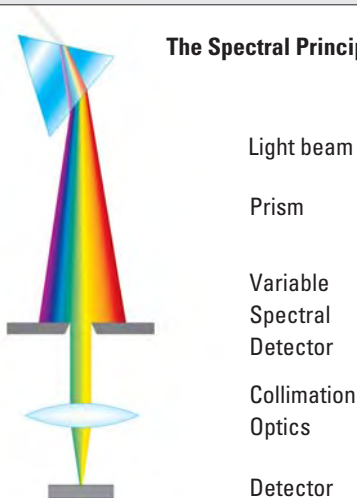


Information from each signal in all optical sections is reconstructed by intelligent software into excellent 3D images, resolving the smallest detail of the specimen's structure. To ensure high quality imaging, optimal excitation is provided by up to four solid-state lasers with 488, 532 and 635 nm lines for common dyes. The broad range of applications is extended by the 405 nm laser option for nuclear staining.

Maximum signal efficiency by spectral detection

Maximize the signal independent from barriers posed by fixed filters and tune freely the emission band from 430 nm to 750 nm. Cross-talk of different dyes in one sample is prevented when tuning the spectral detector precisely in 10 nm steps to the respective dye. For unrivalled detection efficiency, the Leica TCS LSI uses a

The Spectral Principle



prism spectral detector. Minimize bleaching and cell damage by optimizing the detection range and reduce the excitation power via Acousto-Optical Tuneable Filter (AOTF).

Highly innovative

Zoom freely in and out, switching between overview and smallest detail without changing the objectives. The Leica Z16 APO A 16:1 super zoom offers the largest magnification range from 0,57x to 9,2x, whereas the Z6 APO A ranges from 0,57x to 3.6x – at excellent optical performance. The Z-zoom systems are fully apochromatic and allow to adjust magnification continuously and parallax-free.

Benefit from the motorized versions Z16 APO A and Z6 APO A: Fully software controlled, the magnification can be completely altered without touching the imaging system. To achieve precise focusing for sharpest images over a wide range of 10 mm, all motorized zooms are equipped additionally with a motorized fine focus lens.

Macro and Micro: New dimensions for largest specimen

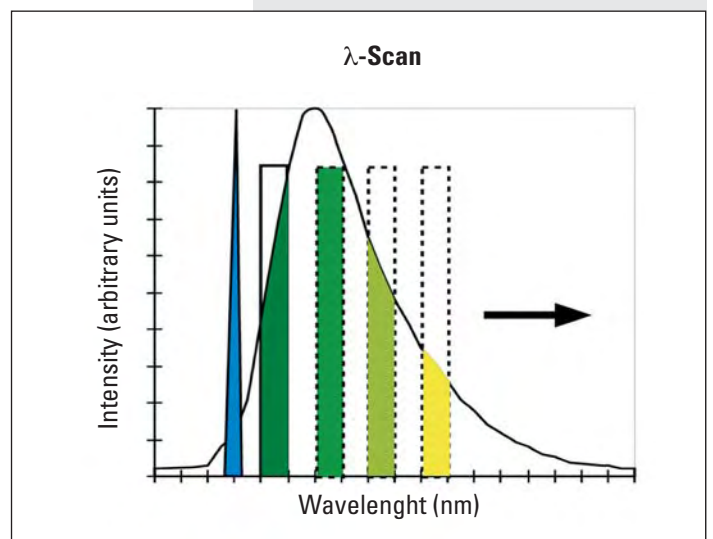
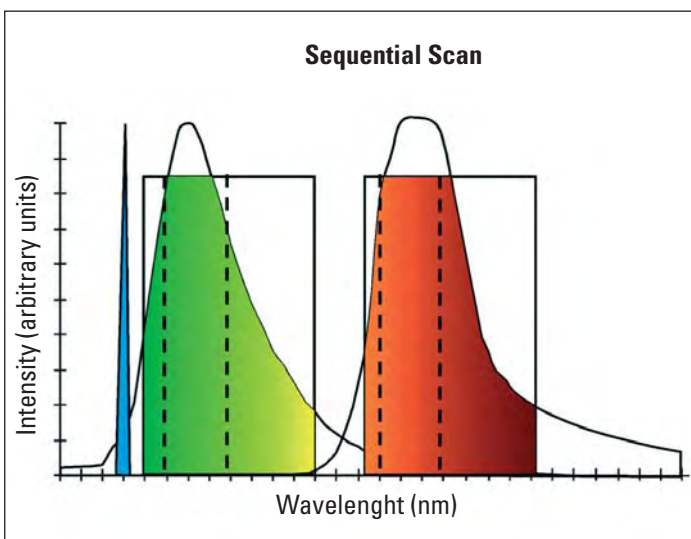
Benefit from the high quality macro objectives of Leica Microsystems. A novelty in confocal imaging: the tremendous working distance (WD) of 97 mm and a field of view (FOV) of 16 mm provided by the 1x apochromatic macro objective. Additionally, classic micro-objectives can be adapted to use the Leica TCS LSI as a classical confocal. With high resolution, high numerical aperture lens systems, finest details at maximum resolution become visible.

New zoom optics

- Change magnification by fingertip
- Continuously variable magnification by 16x
- Motorized
- No objective change required
- Apochromatic, parallax-free optics
- Macro and micro objectives
- 1x, 2x, 5x, 10x, 40x, 63x

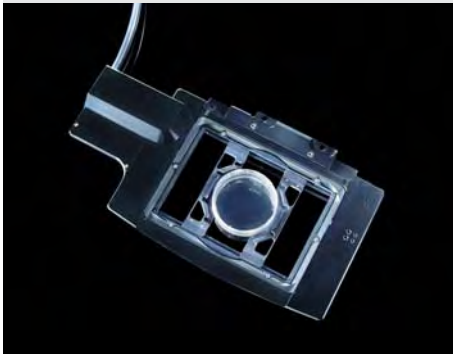


Adjusting of magnification by motorized zoom



Highest Flexibility

- Dynamic confocal imaging
- Spectral band tuning
- 0 – 100% AOTF laser control
- Variable pinhole
- Variable magnification
- Motorized z-zooms
- Full objective band from 1x to 63x
- FOV max: 16 mm
- WD max: 97 mm
- Z-range max: 150 mm



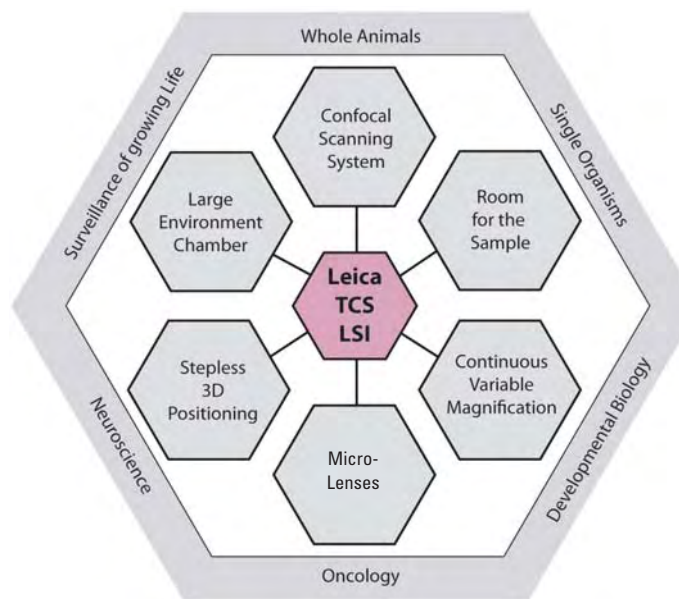
Stage inserts for various applications

Observation and handling of large specimen becomes facile: Overcome the limits of fixed magnifications, small fields of view and low working distances.

Freedom for New Research

Enter new dimensions for flexible applications

The new Leica TCS LSI offers unrivaled flexibility for high resolution imaging. Enjoy the freedom and navigate through your model organism in all three dimensions.



A system flexible for all experiment needs

Observe any specimen straightforward: The large workspace allows for studying even an entire mouse. Select the objective which corresponds best to your experiment. Profit from the fundamentally new design of the laser safety chamber and modify your sample actively by adding a drug to the test population, as even manipulators fit in easily. Through the wide-open wing doors, specimen insertion is facile and handling is comfortable.

Open the door to new applications

Leica TCS LSI is the true first high resolution imaging system offering this extraordinary flexibility. Instead of switching between different instruments, you can do your research and design new experiments with one system. From micro to macro, Leica TCS LSI opens up future for ultimate new research topics.

Easy to use software and workflow-oriented hardware minimizes the training effort and allows scientists to work with the Leica TCS LSI confocal straight away.

Easy to Achieve

Efficient operation for faster success

Easy interfacing: requires less training and enables faster working

From magnification up to z-position, remote control the instrument easily. Minimum training is required even for newcomers. The standardized intuitive user interface of Leica LAS AF enables you to start your work autonomously from the first button click.

Ergonomic software with workflow-oriented screens guides you through your experiment from the first confocal image up to the full 3D reconstruction of your specimen. The effect: Highly efficient imaging and best results on the first shot.

Additional functionality like deconvolution or spectral unmixing ensure application flexibility for the future.

- Minimal training effort
- Large workspace
- Variable magnification
- Workflow orientated
- Fully automated system
- Comfortable operation
- Easy sample access and manipulation
- Compact design



Easy sample handling

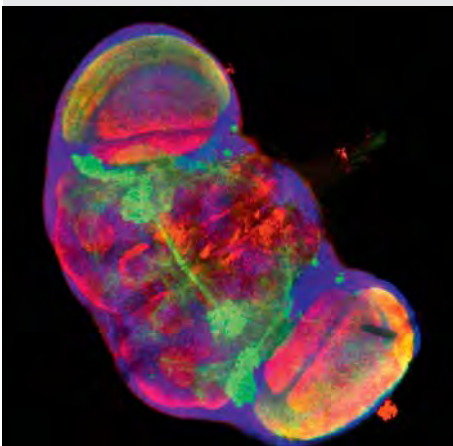
Efficient Operation for Faster Success



Easy confocal imaging:

6 Steps to 3D

1. Start the system
2. Insert specimen, align focus
3. Select instrument settings
4. Define z-range and acquire
5. Calculate 3D image
6. Save and close



Workflow orientated hardware design

The time for preparation, pre-selection and orientation of the specimen reduces enormously as macro and high-resolution confocal are combined in one *in vivo* system.

Saving costs and lab space

The Leica TCS LSI combines both, a macro and a confocal imaging system. The provision of various imaging tools becomes obsolete.

Less stress for the specimen

By avoiding the transportation between different imaging tools, stress to living specimen is reduced, the survival rate increased.

Comfortable handling

Profit from workflow orientated design of the Leica TCS LSI: specimen exchange can be performed fast and secure through wide open wing doors.

Minimal pre-processing

As all sizes fit easily into one system *in vivo*, reduce the number of test organisms by avoiding histopathological tissue processing.

Efficiency for research

Enjoy the efficient operation of the fully automated system: Change magnification quickly on demand and avoid the possible risks during objective changes.

Fast results

Save the time for post processing algorithms as the Leica TCS LSI provides excellent true confocal raw data immediately from your experiment.

Less specimen needed

With Leica TCS LSI, more experiments now can be performed with a single specimen to ensure highest reproducibility and optimal results.

Time Saving

Operate the Leica TCS LSI where your research equipment is, shorten the lane and place the instrument directly in your lab environment.

No need for special room conditions

The dark acrylic glass protects the experiment against light and as the system works at room temperature, additional costs for special room conditions are not required.

A robust system

Stable technology and long lifetime components make the Leica TCS LSI robust and minimize maintenance. Predefined upgrade kits offer extensions for future research.

Efficient operation and excellent results

Brilliant images in short time with less test organisms ensure fast success.

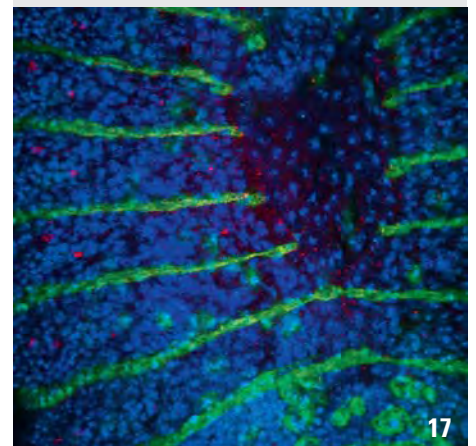
Prepared for the future

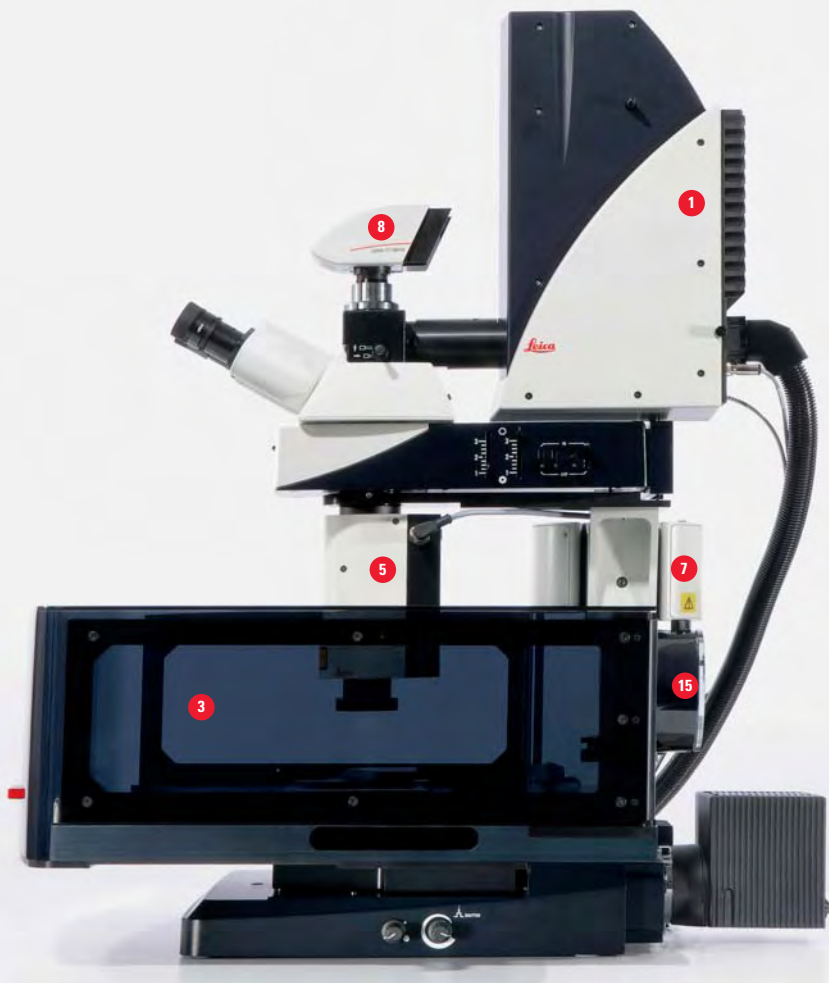
Achieve excellent results from micro to macro today and investigate ultimate new research topics in the future with the new Leica TCS LSI.

Ergonomic software

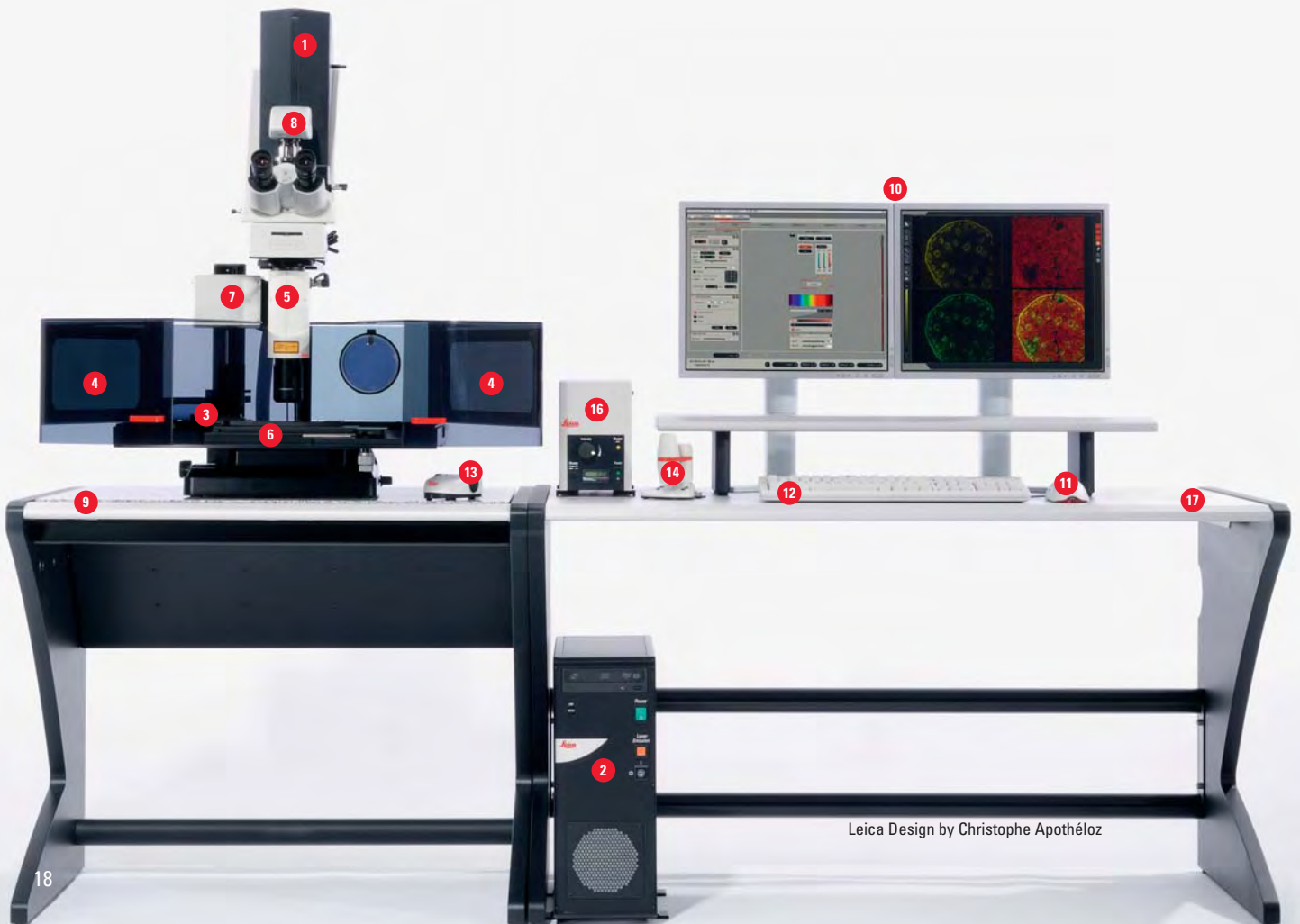
- Common Leica LAS AF platform
- Ergonomic and standardized user interface
- Predefined settings
- Automated long term observation with Advanced Time Lapse
- Easy data transfer
- Analyse specimen with up to eight colors

Leica TSC LSI was developed in co-operation with Jean Luc Vonesch and Didier Hentsch of the Institut de Génétique et de Biologie Moléculaire et Cellulaire (IGBMC), Illkirch, France.





- 1 Confocal scanhead
- 2 Supply unit
- 3 Laser safety chamber
- 4 Wing doors
- 5 Z-zoom, motorized
- 6 SuperZ Galvo stage
- 7 Motor focus drive
- 8 DFC camera option
- 9 Anti-vibration table, passive
- 10 Monitors
- 11 Mouse
- 12 Keyboard
- 13 UMC control
- 14 XY-stage control
- 15 Heat pipe adapter
- 16 EL6000 fluorescence illumination
- 17 Computer table



Leica Design by Christophe Apothélos

Acknowledgements:

1. Mouse transgenic embryo

E10.5 mouse transgenic embryo: EpaxialMyf5 eGFP; immuno-stained for GFP-Alexa 488; the embryonic muscle fibers and the heart are stained with Desmin-Cy3. From top to bottom around 3.5 mm. Courtesy of: Aurélie Jory and Shahragim Tajbakhsh, Cellules Souches et Développement, Institut Pasteur, Paris, France and Imaging centre of IGBMC, IGBMC, Illkirch, France.

2. *Drosophila melanogaster*, head of larvae

Head with nerve system and photoreceptors, Red: Cy3, Green: Alexa 488.

3, 13. Lilly of the valley, rhizome

Convallaria sp.: Rhizome with concentric vascular bundles. Red: cell wall, Green: chloroplasts.

4. Mouse cerebellum

Mus musculus. Cerebellum of mouse P21. Green: Alexa 488, antibodies against GFAP, glial marker, Blue: DAPI. Courtesy of: Giovanni Marchetti, Team E. Georges-Labouesse, Imaging centre of IGBMC, IGBMC, Illkirch, France.

5. Mouse transgenic embryo

Mus musculus. E10.5 mouse transgenic embryo: EpaxialMyf5 eGFP; immuno-stained for GFP-Alexa 488; embryonic muscle fibers and heart stained with Desmin-Cy3. Size from top to bottom: 3.5 mm. Top: RGB-channels. Courtesy of: Aurélie Jory, Cellules Souches et Développement, Institut Pasteur, Paris, France.

6. Chicken, spinal cord

Gallus gallus. Dorsal view of a whole chicken embryo at 10-12 somite-stage, 6h post-electroporation using two DNA constructs: CMV-GFP and neural specific enhancer β -Galactosidase reporter gene. Courtesy of: Isabelle Le Roux and Shahragim Tajbakhsh, Cellules Souches et Développement, Institut Pasteur, Paris, France, Imaging centre of IGBMC, Illkirch, France.

7. *Drosophila melanogaster*, central nerve system

Drosophila melanogaster. Green: GFP. Transgenic fluorescent protein fluorescence in larval CNS. Ventral view, larvae L1.

8, 9. Mouse transgenic embryo, interlimb somites

Five interlimb somites of an E10.5 mouse transgenic embryo: EpaxialMyf5 eGFP; immuno-stained for GFP-Alexa 488; embryonic muscle fibers stained with Desmin-Cy3, the nuclei are revealed with Hoechst Size from top to bottom: 3.5 mm left, 800 μ m right. Courtesy of: Aurélie Jory and Shahragim Tajbakhsh, Cellules Souches et Développement, Institut Pasteur, Paris, France and Imaging centre of IGBMC, IGBMC, Illkirch, France.

10. *Drosophila melanogaster*, head and eye.

Larvae, Head with nerve system, Red: Cy3, Green: Alexa 488, Eye: Photoreceptors with nerve system. Red: Cy3.

12. Zebra fish, novocord development

Danio Rerio. Red: Rhodamine-dextran, Green: GFP, labelling of the notochord. Courtesy of Sophie Dal-Pra, Team B&C Thisse, Imaging centre of IGBMC, IGBMC, Illkirch, France

14. Mouse cerebellum

Mus musculus. Cerebellum of mouse P21. Violet: Alexa488, antibodies against GFAP, glial marker, Blue: DAPI. Courtesy of: Giovanni Marchetti, Team E. Georges-Labouesse, Imaging centre of IGBMC, IGBMC, Illkirch, France

15. Zebra fish

Danio Rerio. Red: Cy3, z-disk staining. Blue: DAPI, nucleoli.

16. Zebra fish development

Danio Rerio. Embryo, T=0h, 6h, 11h, 17h. Bodipy TR. Courtesy of: Jabier Gallego Llamas, Team P. Dolle, Imaging centre of IGBMC, IGBMC, Illkirch, France.

17. *Drosophila melanogaster*, nerve system development.

Larvae Blue: DAPI, nucleoli, Green: Alexa 488, CNS.

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