Fourth (Virtual) Summer School Alternative Methods in Science: towards Fluidic System

Lake Como School of Advanced Studies - 18-19 May 2023 ONLINE SCHOOL

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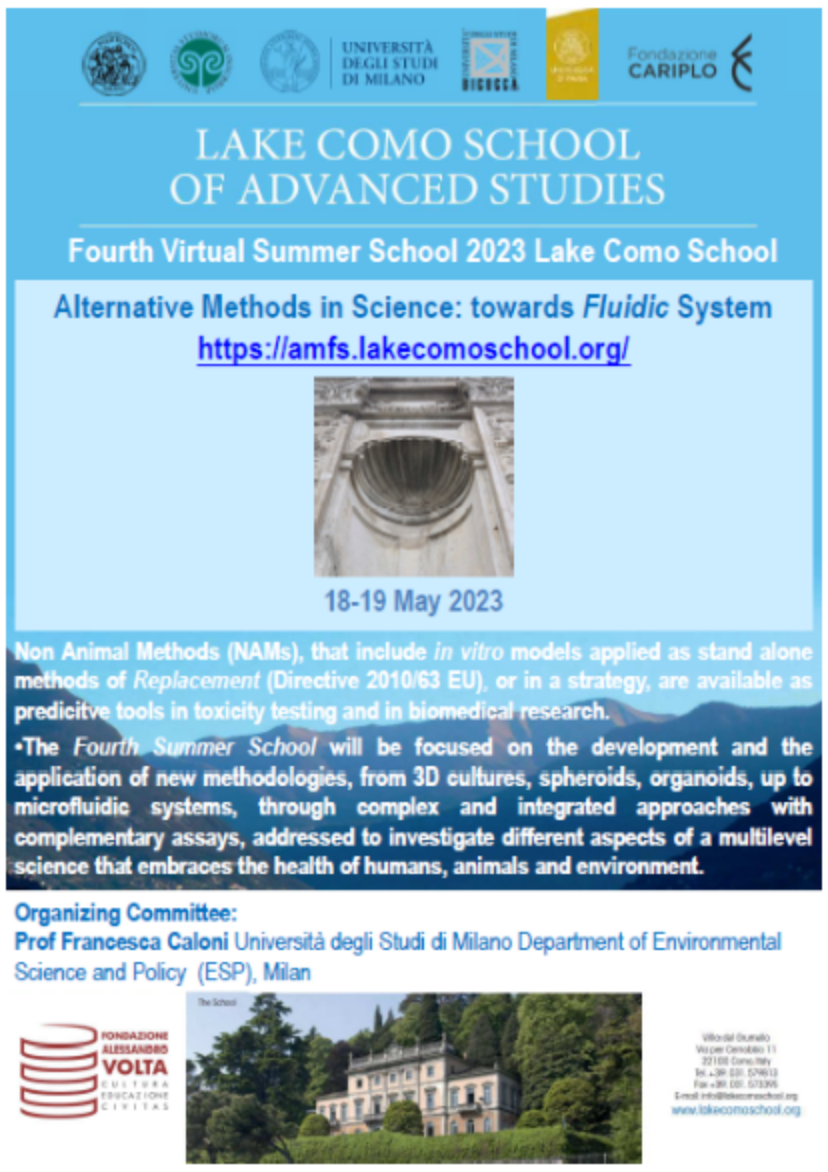

Non Animal Methods (NAMs), that include *in vitro* models applied as stand alone methods of *Replacement* (Directive 2010/63 EU), or in a strategy, are available as predicitve tools in toxicity testing and in biomedical research.

The *Fourth Summer School* will be focused on the development and the application of new methodologies, from 3D cultures, spheroids, organoids, up to microfluidic systems, through complex and integrated approaches with complementary assays, addressed to investigate different aspects of a multilevel science that embraces the health of humans, animals and environment.

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School Director

Prof Francesca Caloni

Università degli Studi di Milano
Department of Environmental Science and Policy

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Program

18 May 2023

9:30 Registration of Participants

10:30 **Alternative Methods in Science: towards *Fluidic* System**

Francesca Caloni- Università degli Studi di Milano Department of Environmental Science and Policy, Milan

11:30 **Animal-product free cell culture and new developments within ALI models**

Arno Gutleb – Luxembourg Institute of Science and Technology (LIST), Luxembourg

12:30-14:00 Lunch

14:00 **Current Challanges in phototoxicity testing**

Helena Kandarova – Institute of Biochemistry and Microbiology Faculty of Chemical and Food Engineering, Slovak Technical University

15:00 ***In vitro* and *ex vivo* Models of Drug-induced Liver Injury**

Hassan Rashidi – Great Ormond Street Institute of Child Health, University College London, London

16:00 Open Debate with the Participants

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19 May 2023

9:30 **Employment of Confocal Laser Scanning Microscope for *in vitro* morphological studies.**

Giulia Ranaldi – Food and Nutrition Research Centre – Council for Agricultural Research and Economics, CREA-AN, Rome

10:30 **Float on: Fast-track development of respiratory tissue**

Doris Wilflingseder – Institute for Hygiene and Medical Microbiology, Medical University of Innsbruck

11:30 **Promoting alternatives to animal experiments as a scientist**

Sonja Von Aulock Editor of ALTEX (Alternatives to Animal Experimentation) **confirmed** (ha accettato di partecipare)

12:30 Open Debate with the Participants

Conclusion

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Speakers

Arno Gutleb

Dr. Arno Gutleb is Group Leader Environmental Health at the Luxembourg Institute of Science and Technology (LIST). The group is developing in vitro assays with a focus on the alveolar region of the lung and inflammation and respiratory sensitization as the main endpoints. He graduated from the University of Veterinary Medicine, Vienna, Austria and holds a PhD (2006) in Environmental Sciences from Wageningen University, The Netherlands. He is a European Registered Toxicologist (ERT) (since 2002). He is Distinguished Professor at the University Iuliu Hatieganu, Cluj, Romania and Visiting Professor at the Universidad Andrés Bello, Santiago de Chile. He is Head of Delegation of Luxembourg to the Working Group of National Coordinators of the Test Guidelines programme (WNT) of the OECD. Since 2020 he is Co-chair of the US-EU NanoEHS CoR.

He founded INIVITROLIZE, a LIST spin-off, in June 2022.

Download the abstract (PDF file): Gutleb

Giulia Ranaldi

Giulia Ranaldi graduated in Biological Sciences at the University La Sapienza of Rome and obtained her PhD in Experimental, Environmental and Occupational Toxicology at the University of Messina. She is Senior Researcher at the Food and Nutrition Research Center of the Italian Council for Agricultural Research and Economics (CREA-AN) in Rome, Italy. Her research activity is mainly focused on the development of *in vitro* models for intestinal absorption and toxicity studies and on the characterization of specific mechanisms of trans-epithelial passage of nutrient, bioactives and xenobiotic. Her work is also aimed to the comprehension of the mechanisms involved in the potential protective effects of food bioactives on intestinal mucosa. Her expertise is also focused on confocal microscopy and imaging analysis for studying morphological cell response to stress or toxic insults .

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Hassan Rashidi

An accomplished stem cell researcher with excellent track record in delivering complex projects within demanding time and cost constraints. Successful in defining hypothesis-driven projects and securing grants. Able to manage budget and lead a team to deliver projects in line with defined objectives. Confident in managing and mitigating risks and issues whilst maintaining progress in line with projects plan. Avid supporter of diversity, equity and inclusion.

Dr Hassan Rashidi
Senior Research Associate
Research Experience

Feb 2021
Senior Research Associate, UCL
• Leading the effort to develop an ectopic hepatic patch supported by Awards from GOSH Charity and Sparks National Call and the Children's Liver Disease Foundation.

Feb 2018 – Feb 2021 Senior Research Associate, UCL
• Developed a novel platform to generate retinal organoids at scale and by using animal-free supplements for the first time.

• Established reprogramming platform to generate and characterise induced pluripotency stem cells.

Oct 2014 – Sep 2017 Research Associate, Uni versity of Edinburgh
• Developed a new protocol to generate human pluripotent stem cell-derived 3D hepatocytes (patented).
• Formulated a new culture medium to stabilise 3D Hepatospheres functions to over a year in culture.

Jan 2011 – Sep 2014
Research Associate, University of Nottingham
• Involved in fabrication of growth factor-loaded microparticles to treat large bone defects.
• Developed a chick embryonic femur culture system to assess the localised effect of released growth factors from manufactured microparticles.

Research Funding

2021 Rosetrees Trust Seedcorn Award £10k, Principal Investigator
2020 GOSH Charity & Sparks National Call £101k, Principal Investigator
2020 UCL Regenerative Medicine TIN Pilot Data £16k, Principal Investigator
2019 Children's Liver Disease Foundation £10k , Principal Investigator
2018 NC3Rs CRACK IT Challenge £100k , Co Investigator

Patent

WO2017072580A1 "Methods for producing Hepat ocytes"
Hagbard L.L., Gunnar C.C., Ericsson J.J., Cameron K.K., Hay D. C. C., Forbes S.S., Rashidi H.

PersonalAwards

2007 Overseas Research Studentship (University of Nottingham, UK, £60k)
2006 International Scholarship (University of Bath, UK, £2k

Education
2007 – 2010 PhD Stem Cell Biology University of Nottingham, United Kingdom
(Supervisor Dr Virginie Sottile)
2006 – 2007 MRes Regenerative Medicine University of Bath, United Kingdom cum laude
2003 – 2005 MSc BiologyUniversity of Leiden, The Netherlands cum laude
2000 – 2002 B Sc Medical Laboratory Science Medical University of Kerman, Iran summa cumlaude
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UCL Institute of Child Health
30 Guilford Street
London WC1N 1EH

Travel Grants
2017
European Association for the Study of the Liver (EASL), £500 Travel grant
2017
European Society of Toxicology, £250 Travel grant
2012
7th International Avian Model Systems Conference, £800 Travel grant
Selected

Publications
1 Froghi, S Hall, A. Hanafi Bin Jalal, A. Andrade, M.O.d. Mohammad Hadi, L. Rashidi, H. G élat, P. Saffari, N. Davidson, B. Quaglia, A. Ultrasound Histotripsy on a Viable Perfused Whole Porcine Liver: Histological Aspects, Including 3D Reconstruction of the Histotripsy Site. Bioengineering 2023 , 10, 278. DOI: 10.3390/bioengineering10030278
2 Froghi S .., de Andrade M O .., Hadi L M .., Gelat P .., Rashidi H .., Quaglia A .., Fuller B .., Saffari N .., Davidson B. Liver Ultrasound Histotripsy: Novel Analysis of the Histotripsy Site Cell Constituents with Implications for Histotripsy Application in Cell Transplantation and Cancer Ther apy. Bioengineering. 2023 ; 10(2):276. DOI: 10.3390/bioengineering10020276
3 R ashidi H.H., Leong Y. C. C., Venner K.K., Pramod H.H., Fei Q.Q., Jones O. J. R. R., Moulding D.D., Sowden J. C. C.,
Generation of 3D retinal tissue from human pluripotent stem cells using a directed small molecule based serum free microwell platform , Sci Rep 12, 6646, 202 2 DOI: 10.1038/s41598 022 10540 1
4 Rashidi H., Hay D.C., Nuclear factor programming improves stem cell derived hepatocyte phenotype, Cell Stem Cell, 29, 5, 2022 , DOI: 10.1016/j.stem.2022.04.009
5 Rashidi H. H., Hay D.C.; Serum Free Production of Three Dimensio nal Hepatospheres from Pluripotent Stem Cells Me thods Mol Biol. 2021 DOI: 10.1007/7651_2021_430 .
6 Lucendo Villarin B., Rashidi H. H., Alhaque S., Fisch er L., Meseguer Ripolles J., Wang Y., O'Farrelly F., Themis M., Hay. D.C., J. Vis. Exp. 2019 ; (149), e59965, DOI 10.3791/59965 .
7 Rashidi H. H., Luu N.T., Alwahsh S.M., Ginai M., Alhaque S., Dong H., ……, Dhawan A., Vallier L., Bradley M., Callanan A., Forbes S.J., Newsome P.N., Hay D.C.; 3D human liver tissue from pluripotent stem cells displays stable phenotype in vitro and supports compromised liver function in vivo . Arch Tox icol. 2018 ; 92(10): 3117 3129, DOI: 10.1007/s00204 018 2280 2 . Citations: 9 2
8 Wang Y., Alhaque S., Cameron K., Meseguer Ripolles J., Lucendo Villarin B., Rash idi H. H., Hay D.C.; J. Vis. Exp., 2017; e55355, DOI: 10.3791/55355(2017)). Citations: 5 5
9 Rashidi H. H., Alhaque S., Szkolnicka D., Flint O., Hay D.C., Fluid shear stress modulation of hepatocyte like cell, Arch Toxicol, 2016 ; 90(7):1757 1761, DOI: 10.1007/s00204 016 1689 8 . Citations: 10 4
10 Ludendo Villarin B.L., Cameron K., Szkolnicka D., Rashidi H. H., Bates N., Kimber S.J., Flint O., Forbes S.J., Iredale J.P., Bradley M., Hay D.C.; Ad Health Mat, 2015 ; 4(12):1820 1825, DOI: 10.1002/adhm.201500391 .
11 Rashidi H. H., Smith E.L., Kanczler J.M., Black C.R., Shakesheff K.M., Oreffo R.O.C.; Plos One, 2015 ; 10(4), DOI: 10.1371/journal.pone.0121653 .
12 Gothard D., Smith E.L., Kanczler J.M., Black C.R., Wells J.A., Roberts C.A., White L.J., Qutachi O., Peto H., Rashidi H. H., Rojo L., Stevens M.M., El Haj A.J., Rose F.R.A.J., Shakesheff K.M., Oreffo

R.O.C.; Plos One, 2015 ; 10(12), DOI: 10.1371/journal.pone.0145080 .
13 Saeed A., Francini N., White L.J., Dixon J., Gould T., Rashidi H. H., Al Ghanami R.C., Hruschka V., Redl H., Saunders B.R., Alexander C., Shakesheff K.M., Adv Mater, 2015 ; 27(4):662 668, DOI: 10.1002/adma.201403626 .
14 Henstock J.R., Rotherham M., Rashidi H. H., Shakesheff K.M., El Haj A.J.; Stem Cell Trans Med, 2 014 ; 3(11):1363 1374, DOI: 10.59 66/sctm.2014 0017 .
15 Rashidi H. H., Strobuecker S., Jackson L., Karla S., Blake A.J., France L., Tufarelli C., Sottile V, Cells Tissue Organs, 2012 ; 195(6):484 494, DOI: 10.1159/00032 9861 .
16 Rashidi H. H., Ellis M.J., Cartmell S.H., Chaudhuri J.B.; Polymers, 2010 ; 2(4):709 718, DOI: 10.3390/polym2040709 .
17 Rashidi H. H., Akhtar M.T., van der Kooy F., Verpoorte R., Duetz W.A.; Appl Environ Microbiol, 2009 ; 75(21):7135 7141, DOI: 10.1128/AEM.01277 09 .

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Doris Wilflingseder

Personal Data	
Place of birth	Innsbruck, Austria
Citizenship	Austrian
Education	
1989	Matura, Bundesgymnasium Sillgasse, Innsbruck, Austria
1997	Master in Zoology, Leopold-Franzens-University of Innsbruck, Austria
2000	PhD in Zoology (Cell Biology, Immunobiology), Leopold-Franzens-University of Innsbruck, Austria
Career History	
2001-2008	Research Assistant, Division of Hygiene and Medical Microbiology, Innsbruck Medical University
2008-2009	Visiting scientist at University College London, Division of Infection and Immunity, collaboration with Prof. Paul Kellam, London, UK
Since 2009 2012-2019	Group leader, Division of Hygiene and Medical Microbiology, MUI and Habilitation in Immunology Associate Professor and Deputy Director, Division of Hygiene and Medical Microbiology, MUI
2020-present	University Professor of Infection Biology
Publications	Number of publications=91 PubMed DW (wilflingseder-d or wilfingseder-d), H-index 30, cited>2500; Google Scholar link
Patents	None
Other Functions	Guest Editor of CELLS Special Edition (MDPI), Reviewer for MRC UK, ARS Journal, Journal of Immunology, ALTEX, Intervirology, board member of the Austrian Society of Allergology and Immunology (ÖGAI), deputy head of the Austrian Society for alternative Biomodels (RepRefRed Society), member of the habilitation committee (Medical University Innsbruck)
Main Areas of Research	• Studying disease mechanisms in optimized human 3D models containing immune elements • Signaling at the interface of infection and inflammation, antigen-presentation, innate humoral immune mechanisms • *In vitro* 3D modeling of human barrier/immune models to study (emerging) human pathogens
Most Important	*CONNECT* faculty at MUI; Günter Weiss (Internal Medicine II, Innsbruck), Dominik Wolf

Collaborators	(Internal Medicine V, Innsbruck); Teunis Geijtenbeek (AMC, NL), Arnaud Moris (INSERM, Paris, France), Ralf Wagner (University of Regensburg, GE), Michael Sixt (IST, Austria), Quentin Sattentau (Sir William Dunn School of Pathology, Oxford, UK), Asier Saez-Cirion (Institut Pasteur, Paris, France), Paul Jennings (AIMMS, Amsterdam, NL)
Teaching and Supervision	I am teaching 11 semester periods per week (=15*45min/period) at the MUI (since 2012; before 2012 I was teaching 4 semester periods per week) Number of PhD students supervise(d): 14; Number of MSc students supervise(d): 5
Awards 1999 2005 2008 2012 **2022**	Award at the European Contest for young scientists on protein purification, Paris, France Hypo-Tirol-Bank Scientific Award Austrian Microbiology Award Award 'Preis der Landeshauptstadt Innsbruck' **Austrian State Award 2021 for Promoting Alternatives to Animal Testing (BMBWF)**
Organisation of Scientific Meetings	Congress President, OEGAI Annual Meeting 2016, ÖGAI Annual Meeting 2016 Scientific Committee, EAACI 2016, http://www.eaaci2016.org/local-organising-committee/ Scientific Committee EUSAAT2019, https://www.eusaat-congress.eu/

10 most important scientific publications

1. Posch W, Bermejo-Jambrina M, Steger M, Witting C, Diem G, Hörtnagl P, Hackl H, Lass-Flörl C, Huber LA, Geijtenbeek TBH, Wilflingseder D*. Complement Potentiates Immune Sensing of HIV-1 and Early Type I Interferon Responses. mBio. 2021 Oct 26;12(5):e0240821.doi: 10.1128/mBio.02408-21. *corresponding author
2. Posch W, Lass-Flörl C, Wilflingseder D,* SARS-CoV-2–infected primary human airway epithelia illustrate mucus hypersecretion. J Allergy Clin Immunol. 2021 Jul 17:S0091-6749(21)01101-5. doi: 10.1016/j.jaci.2021.05.047. *corresponding author
3. Posch W, Vosper J, Zaderer V, Noureen A, Constant S, Bellmann-Weiler R, Lass-Flörl C*, Wilflingseder D,* ColdZyme® maintains integrity in SARS-CoV-2-infected airway epithelia. mBio 2:e00904-21.https://doi.org/10.1128/mBio.00904-21. *corresponding author
4. Posch W*, Vosper J, Noureen A, Zaderer V, Witting C, Bertacchi G, Gstir R, Filipek PA, Bonn GK, Huber LA, Bellmann-Weiler R, Lass-Flörl C, Wilflingseder D*. C5aR inhibition of non-immune cells suppresses inflammation and maintains epithelial integrity in SARS-CoV-2-infected primary human airway epithelia, J Allergy Clin Immunol. 2021 Apr 11;S0091-6749(21)00560-1. doi: 10.1016/j.jaci.2021.03.038. *corresponding author
5. Luvanda MK, Posch W, Noureen A, Lafon E, Zaderer V, Lass-Flörl C, Wilflingseder D*. Dexamethasone Creates a Suppressive Microenvironment and Promotes Aspergillus fumigatus Invasion in a Human 3D Epithelial/Immune Respiratory Model. J Fungi (Basel) 2021 Mar 18;7(3):221. doi: 10.3390/jof7030221. *corresponding author
6. Nijmeijer BM, Bermejo-Jambrina M, Kaptein TM, Ribeiro CMS, Wilflingseder D*, Geijtenbeek TBH*. HIV-1 subverts the complement system in semen to enhance viral transmission. Mucosal Immunol. 2021 Feb 10. doi: 10.1038/s41385-021-00376-9. Online ahead of print. PMID: 33568786 *corresponding author
7. Zaderer V, Herrmann M, Lass-Flörl C, Posch W, Wilflingseder D*. (2019) Turning the World Upside-Down in Cellulose for Improved Culturing and Imaging of Respiratory Challenges Within a Human 3D Model. Cells.2019 Oct 21;8(10). doi: 10.3390/cells8101292. PubMed PMID: 31640299; PubMed Central PMCID: PMC6830077. *corresponding author.
8. Posch W, Steger M, Knackmuss U, Blatzer M, Baldauf HM, Doppler W, White TE, Hörtnagl P, Diaz-Griffero F, Lass-Flörl C, Hackl H, Moris A, Keppler OT, Wilflingseder D*. (2015). Complement-Opsonized HIV-1 Overcomes Restriction in Dendritic Cells. PLoS Pathog. 11(6):e1005005. doi: 10.1371/journal.ppat.1005005. eCollection 2015 Jun. PubMed PMID: 26121641; PubMed Central PMCID: PMC4485899. *corresponding author.
9. Wilflingseder D, Schroll A, Hackl H, Gallasch R, Frampton D, Lass-Flörl C, Pancino G, Saez-Cirion A, Lambotte O, Weiss L, Kellam P, Trajanoski Z, Geijtenbeek T, Weiss G, Posch W. (2015). Immediate T-Helper 17 Polarization Upon Triggering CD11b/c on HIV-Exposed Dendritic Cells. J Infect Dis. 212(1):44-56. doi: 10.1093/infdis/jiv014. Epub 2015 Jan 12. PubMed PMID: 25583169.
10. Posch W, Cardinaud S, Hamimi C, Fletcher A, Mühlbacher A, Loacker K, Eichberger P, Dierich MP, Pancino G, Lass-Flörl C, Moris A, Saez-Cirion A, Wilflingseder D*. (2012) Antibodies attenuate the capacity of dendritic cells to stimulate HIV-specific cytotoxic T lymphocytes. J Allergy Clin Immunol. 2012 Dec;130(6):1368-74.e2. doi: 10.1016/j.jaci.2012.08.025. Epub 2012 Oct 11. PubMed PMID: 23063584. *corresponding author.

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Helena Kandarova

Helena Kandarova, ERT, is a highly accomplished in vitro toxicologist with over 20 years of experience in the field. Dr. Kandarova earned her Ph.D. in Biology, Chemistry and Pharmacy from the Freie Universität Berlin, Germany and is a European Registered Toxicologist (ERT). Previously, she served as the Director of MatTek In Vitro Life Science Laboratories, where she led the research focusing on the development and validation of in vitro testing methods for risk and safety assessment of chemicals, cosmetics and medical devices. Currently, she is the Director of the Institute of Experimental Pharmacology and Toxicology (IEFT) at the Slovak Academy of Sciences, and a Lecturer at the Institute for Biochemistry and Microbiology at the Faculty of Chemical and Food Technology in Bratislava, Slovakia. Dr. Kandarova's areas of expertise include the development and validation of alternative methods to animal testing in toxicology, with a focus on topical toxicity testing. Dr. Kandarova holds multiple pro-bono positions, including President of the European Society of Toxicology In Vitro (ESTIV), Vice-president of the Slovak Society of Toxicology (SETOX), Chair of the Slovak National Platform for 3Rs (SNP3Rs), EPAA Mirror Group Member, Nominated national expert in the OECD expert groups, National representative at EURL ECVAM PARERE activities, and representative of Slovak NETVAL laboratory. Dr. Kandarova is a recipient of numerous prestigious awards, including the EUROTOX Lecture Award, Commemorative Medal from the Society of Toxicologists of Ukraine, Bjorn Ekwall Memorial Award, Doerenkamp-Zbinden Foundation Award, and Lush prize (commended project).

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Protetto: School Materials

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