Curriculum Vitae

Name:	Oliver Distler
Date of birth:	03.11.1968
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Education

2016	Full Professor of Rheumatology, University of Zurich, Switzerland
2013	Professor ad personam at the University of Zürich, Switzerland
2012	Certificate of Advanced Studies in Healthcare Management, University of St. Gallen, Switzerland
2006	Specialization in Rheumatology
2005	Privatdozent at the University of Zurich, Switzerland
2004	Specialization in Internal Medicine
1998	Doctor of Medicine (Dr. med.)
1989-1995	Medical student at the University of Erlangen, Germany and Duke University, North Carolina, USA

Employment history

2015-2017	Adjunct Professor, University of Florence, Italy
2015	Visiting Professor, Stanford University, USA
2012	Visiting Professor, University of Gothenburg, Sweden
2009-2016	Senior Attending Physician (Leitender Arzt) and Director Scleroderma Program, Department of Rheumatology, University Hospital Zurich, Switzerland
2006-2009	Attending Physician (Oberarzt), Department of Rheumatology, University Hospital Zurich, Switzerland
2002-2006	Resident at the Departments of Clinical Immunology and Rheumatology, University Hospital Zurich, Switzerland
1998-2002	Postdoc at the Center of Experimental Rheumatology, Department of Rheumatology, and Department of Clinical Immunology, University of Zurich, Switzerland
1996-1998	Intern/Resident at the Department of Internal Medicine II, Bamberg and the Department of Internal Medicine I, University of Regensburg, Germany

Institutional responsibilities

2016-	Professor, University of Zurich, Switzerland; Chairman Department of Rheumatology, University Hospital Zurich and Balgrist University Hospital, Switzerland
2016-	Chairman Center of Experimental Rheumatology, University of Zurich, Switzerland
2018-	Board Member, Faculty of Medicine, University of Zurich
2018-2021	Head of Business Division, Traumatology-Dermatology-Rheumatology-Plastic Surgery and Emergency Medicine (TDR), University Hospital Zurich, Switzerland
2025	Head ad interim Department of research and teaching in clinical immunology and allergology, University Hospital Zurich

Funded research projects (currently running, O. Distler as PI or Co-PI)

2017-2024	Skintegrity.ch, Flagship Project UZH-ETH. Topic: Systemic sclerosis.
2019-2024	Clinical Research Priority Program (CRPP) at the University of Zurich. Topic: Pain - from phenotypes to mechanisms.
2020-2023	Stiftung für wissenschaftliche Forschung an der Universität Zürich (STWF). Topic: Die Rolle von CD4 T-Zellen in autoimmuner pulmonal-arterieller Hypertonie
2021-2024	SNF. Topic: Patient journey analysis for medical knowledge discovery and clinical decision making.
2021-2025	SNF. Topic: Responsive microbubbles as molecular ultrasound contrast agents.
2022-2024	Innosuisse. Topic: Preclinical development of an innovative drug candidate, TOP-V122, for the treatment of lung fibrosis.
2023-2026	Zürcher Rheumastiftung. Topic: Infrastructur grant Department of Rheumatology.

Supervision of graduate students and postdoctoral fellows (Ongoing)

Research group leaders: PD Dr. Przemyslaw Blyszczuk, Prof. Dr. Florian Brunner, Prof. Dr. Adrian Ciurea, PD Dr. Stefan Dudli, Prof. Dr. Gabriela Kania, PD Dr. Bojana Müller, Prof. Dr. Caroline Ospelt, Prof. Dr. Christof Seiler

Postdoctoral fellows/Attending physicians with research activities: PD Dr. Mike Becker, Dr. Cosimo Bruni, Dr. Rucsandra Dobrota, PD Dr. Muriel Elhai, Dr. Suzana Jordan, PD Dr. Carina Mihai, Dr. Elena Pachera, Dr. Liubov Petelytska

Reviewing activities (only major journals and institutions listed)

Ad hoc reviewer for all major Rheumatology journals (including the leading journals ARD, A&R, Lancet Rheumatology), for journals from General Internal Medicine and other fields (including NEJM and Lancet), different national and international funding agencies (including e.g. DFG), different foundations (including Pfizer Foundation, Hartmann Müller Foundation) and frequent abstract reviewer for the large international congresses in Rheumatology (including EULAR, ACR, Scleroderma World Congress). Editorial board member of Lancet Rheumatology and Annals of the Rheumatic Diseases (ARD).

Prizes and awards (last 5 years)

11/ 2019 Cloëtta-Award 2019, Foundation of Prof. Dr. Max Cloëtta

Organization of major scientific meetings

- Steering committee of the bi-annual Systemic Sclerosis World Congress since 2010
- Advisory board for the annual European Workshop of Rheumatology Research (EWRR) since 2011
- Program committee of the annual European Alliance of Associations for Rheumatology (EULAR) 2012-2014
- President annual Meeting of the Swiss Society of Rheumatology (SGR) 2014-2018
- Program committee of the EUSTAR educational course on systemic sclerosis 2015-2022
- Founding member of the EULAR study group “pulmonary involvement of rheumatic diseases”

Membership in scientific societies

Since 2014	Member scientific committee Swiss Society of Rheumatology (SGR)
Since 2015	Scientific advisory board GILS (Gruppo Italiano per la Lotta alla Sclerodermia) Foundation
Since 2016	Scientific advisory board of the AbbVie Rheumatology Grant
2016-2022	Member foundation board, Hartmann Müller Foundation
2016-2023	Senate member of the Swiss Academy of Medical Sciences, Representative of the University of Zurich
Since 2016	Member Walter-Siegenthaler-Gesellschaft für Fortschritte in der Inneren Medizin
Since 2017	Member Foundation Board, SCQM (Swiss Clinical Quality Management in Rheumatic Diseases)
Since 2019	Member scientific evaluation board, Pfizer Research Foundation
2019-2022	President of EUSTAR (European Scleroderma Trials and Research Group)
Since 2021	Co-Chair of ERS/EULAR Guidelines (European Respiratory Society)
Since 2021	Chair Executive Committee of the FOREUM Foundation (Foundation for Research in Rheumatology)

Major scientific achievements

My research focus is on systemic sclerosis (SSc), which is a difficult to treat chronic autoimmune disease with high morbidity and mortality. Skin fibrosis and internal organ involvement are the hallmarks of this autoimmune disease. Strengths of my research education and activity are its wide coverage, spanning from a preclinical molecular biology program focusing on the identification and characterization of key molecules and intracellular signaling cascades that are driving the disease process to a translational and clinical program with emphasis on precision medicine and phase 2/3 clinical trial design. This is underlined by significant publications in both preclinical and clinical science in SSc. Our Center has been awarded a EULAR Center of Excellence due to the quality and number of scientific publications, and I and my research had the honor to lead and significantly contribute to this achievement.

As an example for the preclinical molecular biology focused program with translation into clinical applications, we could show that signaling via the Serotonin receptor 2b on fibroblasts is a key mechanism to promote fibrosis in a TGF-b dependent manner in vitro, but also in different animal models of skin fibrosis in vivo (Dees et al, 2011). These promising results led us to perform a proof of concept clinical study in patients with SSc using biomarkers as the primary endpoint. In the investigator-initiated study, we found strong effects on key features of fibrosis confirming the animal studies (Distler et al, paper in preparation). In collaboration with an industry partner, we are now designing a phase 2b registration study confirming our findings. This international, multicenter study is coordinated by me and our team.

Another focus in the laboratory are epigenetics and non-coding RNAs. In SSc, we have focused on miRNAs as a class of non-coding RNAs. We were the first to show that miR-29 is down-regulated in SSc by TGF-β, PDGF-B, and IL-4 and directly contributes to fibrosis by targeting collagen mRNA (Maurer et al, 2010). This resulted in a patent filed for the use of miR-29 in scleroderma. Furthermore, we have characterized additional miRNAs such as miR-193b, miR-125b and miR-145 as important posttranscriptional regulators in SSc contributing to diverse pathophysiological processes like vasculopathy and fibrosis (Iwamoto et al 2014, Kozlova et al, 2019). Recently, we have identified the novel long non-coding RNA H19X as a key mediator of TGFb profibrotic effects in a variety of fibrotic conditions. Knock-down of H19X prevented the profibrotic effects of TGFb. RNA Sequencing and ChiRP-Seq showed that these

effects are mediated by steric interaction of H19X with the gene DDIT4L, which is a newly identified collagen inhibitory factor (Pachera et al, 2020).

Our laboratory has been centrally involved in the identification and characterization of animal models of SSc. Animal models are an important part of a preclinical program to evaluate probability of success for clinical trials. For example, there was until recently no animal model available that resembled the vascular changes in human SSc. The further characterization and validation of Fra-2 tg mice enabled the use of this animal model as a preclinical model for both the vascular and fibrotic manifestations of SSc, and it is now one of the most frequently used models for SSc. We could show that these mice develop skin fibrosis likely mediated by initial apoptosis of endothelial cells, and that the vascular lesions largely resembles finding observed in human SSc tissues (Maurer et al, 2009; Maurer et al, 2012). In addition, my group showed that VEGF tg mice develop skin fibrosis in a dose-dependent manner and are more susceptible to inducible models of fibrosis than control wt mice (Maurer et al, 2014).

Translation of our findings into potential clinical applications has always been a focus of our research. This includes optimization of animal models for their translation into clinical applications. We had observed that some of our targets for intervention showed promising results in the animal models, but did not show effects in human proof of concept studies. Using the example of tyrosine kinase inhibitors (Distler, 2007), we could show that the anti-fibrotic effects were strongly depending on the level of activation of the targets, and that in the human disease, target activation was often much lower than in the used animal models (Maurer et al, 2013). This led to change in the use of animal models in preclinical characterization and to updated recommendations how to use animal models in SSc (Jordan et al, 2013). It also highlighted the importance of a stronger focus on examination of target activation in human biosamples as a predictor of successful clinical trials. This approach resulted into a number of studies addressing molecular imaging. In this Sinergia funded program, we could show that molecular imaging using SPECT or PET/CT in mouse models of SSc allows individual identification of activated pathway involving folate receptor beta (FR-β) and integrin avβ3, paving the way for precision medicine approached against these pathways (Schniering et al, 2019).

Finally, our group has contributed to the optimization of clinical trial design leading to changes in the way clinical trials are conducted in SSc. Specifically, we could show by using large patient's numbers from the EUSTAR registry that in randomized clinical trials targeting skin fibrosis, a lower extent of skin fibrosis is necessary to enrich the trials for patients with progressive skin fibrosis (Maurer et al 2015; Dobrota et al, 2016). We also provided a core et of variables for enrichment of patients that show progression of the overall disease and specific organ involvements (Becker et al 2019) and factors to identify patients with progressive interstitial lung disease (ILD) in the early, mild phase of the disease as well as in later stages (Wu et al, 2018; Hoffmann-Vold et al, 2021). We also worked on different serum biomarkers to predict worsening of skin and lung progression in SSc with the aim to enrich trials for progressive patients and identify patients at need of treatment (Dobrota and Jordan et al, 2021). These and other findings contributed to the design of randomized placebo-controlled trials (Khanna et al, 2020) including a very large international randomized placebo-controlled trial with the multi-tyrosine kinase inhibitor nintedanib for SSc-ILD. It could be shown that nintedanib significantly slows the progression of SSc-ILD over placebo (Distler et al, 2019). These results led to the first FDA approved targeted therapy for SSc-associated interstitial lung disease (ILD).

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