# Sumeet Pal Singh | PhD

### **Personal Details**

Birth Date: August 12, 1985

Nationality: Indian
Family Status: Married



# **Research Experience**

**Assistant Professor (Tenured)** 

2022-Onwards

Institut de Recherche Interdisciplinaire en Biologie Humaine et Moléculaire (IRIBHM)

Université Libre de Bruxelles (ULB)

Brussels, Belgium

Group Members: Three PhD Candidates + One Technician.

Project title: Regenerative and Stress Biology.

### Research Group Leader

2019-2022

Institut de Recherche Interdisciplinaire en Biologie Humaine et Moléculaire (IRIBHM)

Université Libre de Bruxelles (ULB)

Brussels, Belgium

## **Education / Training**

Post-Doctoral Fellow

2014-2019

DFG Center for Regenerative Therapies Dresden

Dresden, Germany

Research Advisor: Nikolay Ninov, Ph.D.

Project title: Cellular and Epigenetic Dynamics in  $\beta$ -cell during Development, Regeneration and

Diabetes.

**Post-Doctoral Fellow** 

2013-2014

Max Planck Institute of Molecular Cell Biology and Genetics

Dresden, Germany

Research Advisor: Jochen Rink, Ph.D.

Project title: Live Imaging Stem Cell Dynamics during Growth and Regeneration.

**PhD**Duke University

2008–2013

Research Advisor: Kenneth D. Poss, Ph.D.

Durham, USA

Thesis Title: Cellular and Molecular Determinants of Zebrafish Fin Osteoblast Regeneration.

B. Tech., Biological Sciences and Bioengineering

2004-2008

Indian Institute of Technology (IIT)

Kanpur, India

Grade: 8.7 / 10

### Lab's Vision

The Singh Lab @ IRIBHM, ULB focusses on regenerative and stress biology. We are interested in understanding the ability of organs to recover from injuries and stress. For example, we are able to heal a cut to our finger, even if it happens multiple times. Our blood regenerates after blood donation within a day or two. In ancient Greek mythology, Prometheus was sentenced to having half of his liver eaten by an eagle every day, but the liver would regenerate during the night – highlighting the almost infinite regenerative capacity of the liver. We are fascinated by such robustness in regenerative systems - which are a hallmark of a dynamic biological system.

To understand the robustness of biological systems, we explore two main themes: **plasticity and adaptation**.

For our experimental model, we use Zebrafish, which posses amazing regenerative abilities. It is able to recover from complete loss of bone cells or pancreatic beta-cells. We utilize its super-natural regenerative ability to explore our themes, with the hope that the lessons we learn can be translated to improve outcomes of human injury.

### **Contribution to Science**

### 1. Cellular plasticity during regeneration

During my doctoral studies, I focused on the cellular source of bone-synthesizing osteoblast cells in the zebrafish fin. I developed a model for depleting the osteoblast population using a cell-specific and inducible ablation strategy. This revealed that the contribution of osteoblasts to bone and fin regeneration was redundant, and that the mesenchymal fibroblasts could contribute in their absence, demonstrating cellular plasticity during regeneration.

As a post-doctoral researcher, I embarked on understanding the plasticity in the pancreatic  $\beta$ -cell regeneration. Zebrafish, can recover from complete  $\beta$ -cell destruction. In contrast, human  $\beta$ -cells do not recover after massive death, which in turn leads to Type 1 or Type 2 diabetes. For this, we carried out single-cell mRNA-Sequencing (scRNASeq) of the endocrine islets after  $\beta$ -cell ablation. This lead to an intriguing observation that suggested plasticity within the endocrine population. We documented a new progenitor source for  $\beta$ -cells. Specifically, we observed a sub-population of the pancreatic  $\delta$ -cells were capable of trans-differentiating into  $\beta$ -cells.

(a) **Singh SP**, Holdway JE, Poss KD.

Regeneration of amputated zebrafish fin rays from de novo osteoblasts.

Developmental Cell: Apr 17; doi:10.1016/j.devcel.2012.03.006

2012

(b) **Singh SP\***, Chawla P\*, et al.

\*Equal contribution

A single-cell atlas of de novo beta-cell regeneration reveals the contribution of hybrid beta/delta cells to diabetes recovery in zebrafish.

**Development**: January 28; doi:10.1242/dev.199853

2022

#### 2. Adaptation to stress response

A major driver of evolutionary selection is the adaptation to starvation as animals in the wild face uncertain food supply. Adaptation to periods of famine shape physiology in a variety of species: fatty liver in migratory birds, high blood sugar in seals and insulin resistance (IR) in hibernating bears. In the first independent publication from my group, we demonstrated that the zebrafish liver accumulates lipid droplets in response to starvation. Hepatic steatosis, in this case,

creates an energy reservoir that allows survival during long-term caloric deprivation. We studied this "natural" mode of liver steatosis to uncover the mechanisms underlying its induction and resolution, identifying insulin-driven calcium signaling as a regulator of fatty liver. Other metabolic stressors, such as high-fat diet and alcohol both cause fatty liver, medically referred to as Nonalcoholic Fatty Liver (NAFL) and Alcoholic Fatty Liver (AFL), respectively. As steatosis is the first step towards liver disease, we are currently applying our findings to these clinical significant contexts.

(a) Pozo Morales M, Garteizgogeascoa I, Perazzolo C, Singh SP. In vivo imaging of calcium dynamics in zebrafish hepatocytes.

**Hepatology**: March 01; doi:10.1002/hep.32663

#### 2023

### **Grants Awarded**

#### Research Credit (CDR) - FNRS

2022

Learning from the extreme: Starvation induces non-alcoholic fatty liver in zebrafish, which is resolved by mobilization of endo-lysosomal calcium stores.

#### Jaumotte-Demoulin Foundation

2021

Metabolic adaptation to nutritional deprivation.

#### MISU-PROL FNRS Fellow

2021-2022

Regulators of cellular plasticity in endocrine organs.

#### Jaumotte-Demoulin Foundation

2020

Regulators of metabolic cell death.

#### **ULB ERC Support**

2020

Financial support for reaching second start of the ERC Competition.

#### MISU FNRS Fellow

2019-2021

How multi-tasking segregates homogenous cellular societies.

# How multi-tasking segregates homogenous cellular societies.

2019-2021

#### EFSD/Lilly Young Investigator Research Award

2018-2019

The role of tetraspanin-7, an islet autoantigen, in regulating beta-cell functional heterogenity

Deutsche Forschungsgemeinschaft (DFG) Research Fellowship (Declined)

#### **CRTD Postdoctoral Seed Grant**

2016-2017

Dissecting functional heterogeneity in  $\beta$ -cells using Single-cell RNA-Seq

#### **CRTD Postdoctoral Seed Grant**

2015-2016

Inducible Cas9/CRISPR for Conditional Gene Knockouts in Vertebrate Regenerative Model Systems

## **Publications**

# **Preprints**

1. Valiente-Gabioud A, Garteizgogeascoa I, Idziak A, Fabritius A, Angibaud J, Basquin J, Nägerl UV, Singh SP, Griesbeck O.

Fluorescent Sensors for Imaging Interstitial Calcium.

bioRxiv: March 24; doi:10.1101/2023.03.23.533956

2023

2. Ibneeva L, **Singh SP**, Sinha A, Eski SE, Wehner R, Rupp L, Perez-Valencia JA, Gerbaulet A, Reinhardt S, Wobus M, Bonin M, Sancho J, Lund FE, Dahl A, Schmitz M, Bornhaeuser M, Chavakis T, Wielockx B, Grinenko T.

CD38 promotes hematopoietic stem cell dormancy via c-Fos.

bioRxiv: February 08; doi:10.1101/2023.02.08.527614

2023

3. De Faria Da Fonseca B, Barbee C, Romitti M, Eski S E, Gillotay P, Monteyne D, Perez-Morga D, Refetoff S, **Singh SP**, Costagliola S.

Foxe1 orchestrates thyroid and lung cell lineage divergence in mouse stem cell-derived organoids.

bioRxiv: May 16; doi:10.1101/2022.05.16.492074

2022

4. Gillotay P, Romitti M, Dassy B, Haerlingen B, Parakkal MS, De Faria Da Fonseca B, Panos Z G, **Singh SP**, Gerasimos S, Costagliola S.

Nrf2 promotes thyroid development and hormone synthesis.

bioRxiv: March 01; doi:10.1101/2022.02.27.482168

2022

# **Original Research Articles**

 Yu Q, Walters HE, Pasquini G, Singh SP, León-Periñán D, Petzold A, Kesavan P, Subiran C, Garteizgogeascoa I, Knapp D, Wagner A, Bernardos A, Alfonso M, Nadar G, Dahl A, Busskamp V, Martínez-Máñez R, Yun MH.

Cellular senescence modulates progenitor cell expansion during axolotl limb regeneration.

**bioRxiv**: May 16; doi:10.1101/2022.09.01.506196

2022

**Developmental Cell**: Accepted

2023

6. Pozo Morales M, Garteizgogeascoa I, Perazzolo C, **Singh SP**. *In vivo imaging of calcium dynamics in zebrafish hepatocytes.* 

Hepatology: March 01; doi:10.1002/hep.32663

2023

7. Romitti M, Tourneur A, De Faria Da Fonseca B, Doumont G, Gillotay P, Liao X-H, Eski S, E, Van Simaeys G, Chomette L, Lasolle H, Monestier O, Figini Kasprzyk D, Detours V, **Singh SP**, Goldman S, Refetoff S, Costagliola S.

Transplantable human thyroid organoids generated from embryonic stem cells to rescue hypothyroidism.

Nature Communications: November 17; doi:10.1038/s41467-022-34776-7

2022

8. McLaughlin K, Acreman S, Nawaz S, Cutteridge J, Clark A, Knudsen JG, Denwood G, Spigelman AF, Manning Fox JE, **Singh SP**, MacDonald PE, Hastoy B, Zhang Q.

Loss of tetraspanin-7 expression reduces pancreatic  $\beta$ -cell exocytosis Ca2+ sensitivity but has limited effect on systemic metabolism.

Diabetic Medicine: October 20; doi:10.1111/dme.14984

2022

9. Xiao P, Takiishi T, Moretti Violato N, Licata G, Dotta F, Sebastiani G, Marselli L, **Singh SP**, Sze M, Van Loo G, Dejardin E, Gurzov EN, Cardozo AK.

NF-kappaB-inducing kinase (NIK) is activated in pancreatic beta-cells but does not contribute to the development of diabetes.

**Cell Death & Disease**: May 19; doi:10.1038/s41419-022-04931-5

2022

10. Nahaboo W, Eski SE, Despin-Guitard E, Vermeersch M, Saykali B, Monteyne D, Gabriele S, Magin TM, Schwarz N, Leube RE, Zwijsen A, Perez-Morga D, **Singh SP**, Migeotte I. Keratin filaments mediate the expansion of extra-embryonic membranes in the post-gastrulation mouse embryo.

**EMBO Journal**: March 10; doi:10.15252/embj.2021108747

2022

11. **Singh SP\***, Chawla P\*, Hnatiuk A, Kamel M, Silva LD, Spanjard B, Eski SE, Janjuha S, Olivares P, Kayisoglu O, Rost F, Blasche J, Krankel A, Petzold A, Kurth T, Reinhardt S, Junker JP, Ninov N.

\*Equal contribution

A single-cell atlas of de novo beta-cell regeneration reveals the contribution of hybrid beta/delta cells to diabetes recovery in zebrafish.

**Development**: January 28; doi:10.1242/dev.199853

2022

12. Elvira B, Vandenbempt V, Bauza-Martinez J, Crutzen R, Negueruela J, Ibrahim H, Winder M, Brahma M, Vekeriotaite B, Martens P-J, **Singh SP**, Rossello F, Lybaert P, Otonkoski T, Gysemans C, Wu W, Gurzov E.

PTPN2 regulates the interferon signalling and endoplasmic reticulum stress response in pancreatic beta-cells in autoimmune diabetes.

**Diabetes**: January 19; doi:10.2337/db21-0443

2022

13. Romitti M§\*, Eski SE\*, Fonseca BF, **Singh SP**§, Costagliola S§.

\*Equal contribution

§Co-Corresponding Author

Single-cell trajectory inference guided enhancement of thyroid maturation in vitro using TGF-beta inhibition.

Frontiers in Endocrinology: May 31; doi:10.3389/fendo.2021.657195

2021

14. Pronobis MI, Zheng S, **Singh SP**, Goldman JA, Poss KD.

In vivo proximity labeling identifies cardiomyocyte protein networks during zebrafish heart regeneration.

**eLife**: March 25; doi:10.7554/eLife.66079

2021

15. Gillotay P, Shankar MP, Haerlingen B, Eski SE, Pozo-Morales M, Garteizgogeascoa I, Reinhardt S, Kraenkel A, Blaesche J, Petzold A, Ninov N, Kesavan G, Lange C, Brand M, Detours V, Costagliola S§, **Singh SP**§.

§Co-Corresponding Author

Single-cell transcriptome analysis reveals thyrocytediversity in the zebrafish thyroid gland.

**EMBO Reports**: November 06; doi:10.15252/embr.202050612

2020

Featured as Cover Image

16. Mathiah N, Despin-Guitard E, Stower M, Nahanoo W, Eski SE, **Singh SP**, Srinivas S, Migeotte I Asymmetry in the frequency and position of mitosis in the mouse embryo epiblast at gastrulation.

**EMBO Reports**: October 05; doi:10.15252/embr.202050944

2020

17. Eski SE, Dubois C, Singh SP§.

§Corresponding Author

Nuclei Isolation from Whole Tissue using a Detergent and Enzyme-Free Method.

**JoVE**: June 24; doi:10.3791/61471

2020

Chen LS, Singh SP, Mueller G, Bornstein SR, Kanczkowski W.
 Transcriptional analysis of sepsis-induced activation and damage of the adrenal microvascular cells.

 Frontiers in Endocrinology: January 22; doi:10.3389/fendo.2019.00944

19. Salem V, Silva LD, Suba K, Georgiadou E, Gharavy SNM, Akhtar N, Martin-Alonso A, Gaboriau DCA, Rothery SM, Stylianides T, Carrat G, Pullen TJ, **Singh SP**, Hodson DJ, Leclerc I, Shapiro AMJ, Marchetti P, Briant LJB, Distaso W, Ninov N, Rutter GA. Leader beta-cells coordinate Ca2+ dynamics across pancreatic islets in vivo.

Nature Metabolism: June 14; doi:10.1038/s42255-019-0075-2

2019

- 20. Chen LS, **Singh SP**, Schuster M, Grinenko T, Bornstein SR, Kanczkowski W. *RNA-seq analysis of LPS-induced transcriptional changes and its possible implications for the adrenal gland dysregulation during sepsis.* 
  - **J. Steroid Biochem. Mol. Biol**: November 29; doi:10.1016/j.jsbmb.2019.04.009
- 21. **Singh SP**§, Janjuha S, Chaudhuri S, Reinhardt S, Dietz S, Eugster A, Bilgin H, Korkmaz S, Zararsiz G, Ninov N, Reid JE.

§Corresponding Author

Machine learning based classification of cells into chronological stages using single-cell transcriptomics.

Scientific Reports: November 21; doi:10.1038/s41598-018-35218-5

2018

22. Cox BD, Simone AD, Tornini VA, **Singh SP**, Talia SD, Poss KD. In Toto imaging of dynamic osteoblast behaviors in regenerating skeletal bone.

Current Biology: November 29; doi:10.1016/j.cub.2018.10.052

2018

23. Janjuha S\*, **Singh SP\***, Ninov N.

\*Equal contribution

Analysis of Beta-cell Function Using Single-cell Resolution Calcium Imaging in Zebrafish Islets.

**JoVE**: July 03; doi:10.3791/57851

2018

- 24. Janjuha S\*, **Singh SP\***, Tsakmaki A, Gharavy SNM, Murawala P, Konantz J, Birke S, Hodson DJ, Rutter GA, Bewick GA, Ninov N.
  - \*Equal contribution

Age-related islet inflammation marks the proliferative decline of pancreatic beta-cells in zebrafish.

eLife: April 06; doi:10.7554/eLife.32965

2018

25. **Singh SP**, Janjuha S, Hartmann T, Kayisoglu O, Konantz J, Birke S, Murawala P, Alfar EAA, Murata K, Eugster A, Tsuji N, Morrissey ER, Brand M, Ninov N. *Different developmental histories of beta-cells generate functional and proliferative heterogeneity during islet growth.* 

Nature Communications: September 22; doi:10.1038/s41467-017-00461-3

2017

26. Fei JF, Knapp D, Schuez M, Murawala P, Zou Y, **Singh SP**, Drechsel D, Tanaka EM. Tissue and time-directed electroporation of CAS9 protein-gRNA complexes in vivo yields efficient multigene knockout for studying gene function in regeneration.

npj Regenerative Medicine: June 1; doi:10.1038/npjregenmed.2016.2

2016

27. **Singh SP**, Holdway JE, Poss KD.

Regeneration of amputated zebrafish fin rays from de novo osteoblasts.

Developmental Cell: Apr 17; doi:10.1016/j.devcel.2012.03.006

2012

28. Wang JH, Panáková D, Kikuchi K, Holdway JE, Gemberling M, Burris JS, **Singh SP**, Dickson AL, Lin YF, Sabeh MK, Werdich AA, Yelon D, Macrae CA, Poss KD.

The regenerative capacity of zebrafish reverses cardiac failure caused by genetic cardiomyocyte depletion.

**Development**: Aug 15; doi:10.1242/dev.068601

2011

### **Review Article**

29. Singh SP, Ninov N.

The triumvirate of beta-cell regeneration: Solutions and bottlenecks to curing diabetes.

Int. J. Dev. Biol.: June 28; doi: 10.1387/ijdb.180067nn

2018

# **Book Chapter**

30. **Singh SP**, Ninov N.

Multicolor labeling and tracing of pancreatic beta-cell proliferation in zebrafish.

Animal Models of Diabetes: Methods and Protocols

Editor: King, Aileen. Publisher: Springer US. doi:10.1007/978-1-0716-0385-7\_12

2020

### **Editorial**

31. Costagliola S, Singh SP.

Emerging Technologies in Thyroid Biology: Pushing the Frontiers of Thyroid Research.

Molecular and Cellular Endocrinology.: May 01; doi:10.1016/j.mce.2023.111912

2023

# **Conference Talks / Seminars (Last Five Years)**

Zebrafish as a model of human thyroid disorders

Seminar: University of Wisconsin-Madison

Single-cell endocrinology

Conference raiks / Seminars (East rive rears)	
Seminar: Indian Institute of Technology (IIT), Kanpur Mechanisms of starvation resistance	Kanpur, India 2023
Seminar: Indian Institute of Technology (IIT), Delhi Mechanisms of starvation resistance	New Delhi, India 2023
Seminar: Biology Department, KU Leuven Resolution of hepatic steatotsis in zebrafish	<b>Leuven, Belgium</b> 2022
Belgium Society for Cell and Developmental Biology Resolution of hepatic steatotsis in zebrafish	Brussels, Belgium 2022
Helmholtz Zentrum München Preprint publishing and evolving the peer-review process	<b>Webinar</b> 2022
6th European Zebrafish PI Meeting Speaker: Single-cell interactome	Dresden, Germany
Chair: Metabolism and Endocrinology	2022
43rd Annual Meeting of the European Thyroid Association	Milano, Italy*

Madison, USA\*

2021

2021

EMBL-EBI Training with Europe PMC Preprints 101 for authors	<b>Webinar</b> 2021
3rd Italian Zebrafish Meeting (ZFIM) Thyroid Macrophage Interaction	Napoli, Italy* 2021
Seminar: New York University Abu Dhabi Single-cell endocrinology	Abu Dhabi, UAE* 2021
26th Japanese Medaka and Zebrafish Meeting Thyroid Morphogenesis	<b>Chiba, Japan*</b> 2020
<b>4th Challenges in Computational Biology meeting</b> Single Cell Data Analysis	Mainz, Germany* 2020
*In-person meeting moved online due to COVID19	
Interdisciplinary Scientific Seminars - ULB Cooperative Behaviour	Brussels, Belgium 2020
Applied Bioinformatics in Life Sciences (3rd edition)  Machine Learning in Aging	Leuven, Belgium 2020
Awards and Achievements	
10x Genomics Grant Program: Best Abstract	2020
Best Poster Award: CRTD Day	2019
Deutsche Zentrum für Diabetesforschung (DZD) Award: Conference Pr	resentation 2016
Best Talk Award: Genetics and Genomics Departmental Retreat	2012
Best Talk Award: Cell Biology Departmental Retreat	2012
Summer Internship Award: Jawaharlal Nehru Centre for Advanced Scientific	Research 2007
Baljit and Nirmal Dhindsa Scholarship: Highest Grades (Biological Depart	ment) 2005
Academic Excellence Award: Freshman Student	2004
Ongoing Memberships in International Societies	
International Society for Regenerative Biology (ISRB) European Association for the Study of the Liver (EASL) International Zebrafish Society (IZFS) European Zebrafish Society (EZS) European Thyroid Association (ETA) Society for Experimental Biology (SEB) Society for Developmental Biology (SDB) Belgian Society for Cell and Developmental Biology (BSCDB) Belgian Society of Physiology and Pharmacology (PhysPhar-Belgium)	
Scientific Outreach	
ASAPBio Fellow Raise awareness of preprints and encourage their productive use in the life scient	2021 nces
Pint of Science (Belgium) Animal Models in Science	2020
Science Slam (Deutsch) Vorhersage des Zellulären Alters durch Künstliche Intelligenz	2017
Journal Coverage Podcast Audio interviews of scientific authors with recent, important publications	2015–2019

# **Pedagogy**

Instructor, Scientific Communication - 5 credit course 2022-Onwards Medical Department, ULB Brussels, Belgium Instructor, Hands-on Introduction to RNA-Seq 2021 CIVIS (European CIVIC University), ULB Brussels, Belgium **Organizer**, **School Workshop** 2020-2021 International School of Brussels (ISB) Brussels, Belgium Instructor, Online Courses 2020 R and Bioinformatics YouTube Mentor, English Language 2018-2019 Freedom English Academy (FEA) via Skype, India Volunteer, School Student Lab Practical Course 2018 Center for Regenerative Therapies Dresden Dresden, Germany Teaching Assistant (TA), Advanced Topics: Genetics/Genomics 2009

### **Diversity Promotion**

**Duke University** 

Member - Diversity, Equity, and Inclusion (DEI) committee 2020–2022 International Zebrafish Society (IZFS)

Durham, USA