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## APPLICATION FORM

for Abstract Selection Committee Member (representing Basic Science) of the European  
 Pancreatic Club (EPC)

1	<b>Personal data</b>	Name: Rainer Heuchel Username ( <a href="http://www.e-p-c.org">www.e-p-c.org</a> ): raiheu Country: Sweden National Society: not registered
2	<b>Membership</b>	List of years when the applicant was member of EPC (if applicable): 2013, 2015  List of years when the applicant attended the annual EPC meeting (if applicable): 2010, 2011, 2013  List of years when the applicant had communication(s) at the annual main or satellite EPC meeting: 2010 one oral myself, 4 posters), 2011 (2 posters), 2013 (1 oral myself, 2 posters), 2014 (1 poster), 2015 (2 orals by group members, 4 posters)
3	<b>Publications</b>	List of the best 5 original/review papers in international journals:  1) Gerling M, Zhao Y, Nania S, Norberg KJ, Verbeke CS, Englert B, Kuiper RV, Bergstrom A, Hassan M, Neesse A, Lohr JM, <b>Heuchel RL</b> . Real-time assessment of tissue hypoxia in vivo with combined photoacoustics and high-frequency ultrasound. <b><u>Theranostics</u></b> . 2014;4(6):604-13.  2) Longati P, Jia X, Eimer J, Wagman A, Witt MR, Rehnmark S, Verbeke C, Toftgard R, Lohr M, <b>Heuchel RL</b> . 3D pancreatic carcinoma spheroids induce a matrix-rich, chemoresistant phenotype offering a better model for drug testing. <b><u>BMC cancer</u></b> . 2013;13:95.  3) Lonardo E, Hermann PC, Mueller MT, Huber S, Balic A, Miranda-Lorenzo I, Zagorac S, Alcalá S, Rodríguez-Arabaolaza I, Ramirez JC, Torres-Ruiz R, Garcia E, Hidalgo M, Cebrian DA, <b>Heuchel R</b> , Lohr M, Berger F, Bartenstein P, Aicher A, Heeschen C. Nodal/Activin signaling drives self-renewal and tumorigenicity of pancreatic cancer stem cells and provides a target for combined drug therapy. <b><u>Cell stem cell</u></b> . 2011;9(5):433-46.  4) Krampert M, Chirasani SR, Wachs FP, Aigner R, Bogdahn U, Yingling JM, Heldin CH, Aigner L, <b>Heuchel R</b> . Smad7 regulates the adult neural stem/progenitor cell pool in a transforming growth factor beta- and bone morphogenetic protein-independent manner. <b><u>Molecular and cellular biology</u></b> . 2010;30(14):3685-94  5) Nakao A, Afrakhte M, Moren A, Nakayama T, Christian JL, <b>Heuchel R</b> , Itoh

		S, Kawabata M, Heldin NE, Heldin CH, ten Dijke P. Identification of Smad7, a TGFbeta-inducible antagonist of TGF-beta signalling. Nature 1997;389:631-5.
4	<b>Previous positions at EPC or UEG</b>	None yet.

The applicant confirms that she/he

- has read the Open call for Abstract Selection Committee Member (Basic Science) position and fully accept its content
- has adequate time resources for volunteer work
- has good command of spoken and written English

Name

Date: 2015-06-01

*Rainer Heldin*

## CV Rainer Heuchel

### 1. Higher education qualification

Diploma in molecular biology, Zuerich University, Switzerland 1989

### 2. Doctoral degree

University of Zuerich, Switzerland; Ph.D. in molecular biology 1994, (Prof. W. Schaffner)

### 3. Previous positions and periods of appointment.

Postdoctoral Research Fellow, Ludwig Inst. for Cancer Research (LICR), Uppsala 1994-1999

Group Leader (Gene Targeting), Ludwig Inst. for Cancer Research (LICR), Uppsala 1999-2007

### 4. Current position (2008 – present)

Senior researcher, responsible for the Pancreas Cancer Research Lab; Karolinska Institute

### 5. PhD Supervision

Main supervisor

Greger Brodin, PhD-stud at LICR/Uppsala, PhD April 2002

Main supervisor, ongoing

Xuan Li (KI)

Co-supervisor - ongoing:

Jiaqi Huang (KI), Anna Lindahl (KI), Linnea Malgerud (KI)

### 6. Postdoc Supervision

Ying	Zhao	2012-	present
Marco	Gerling	2012-	2014
Immacolata	diGennaro	2011-	2013
Paola	Longati	2008-	2013
Jean-Baptiste	Fini	2008-	2009

Feng	Wang	2008-	2010
Bengt	Rönnberg	2007-	2007
Monika	Krampert	2005-	2007
Shioto	Suzuki	2005-	2007
Camilla	Looman	2004	2006
Ronggui	Li	2003	2005
Henrik	Forsberg	1999-	2000

### 7. Received Research Grants following peer review:

Source	main applicant	start	end	total sum	Co-applicant
Cancerfonden	Rainer Heuchel	2014-01-01	2016-12-31	1800.000	Matthias Löhr - KI
Cancerfonden	Rainer Heuchel	2013-05-01	2013-12-31	650.000	Matthias Löhr - KI
EU	Thomas Gress	2011-01-01	2014-07-31	1880.000	Rainer Heuchel – KI Matthias Löhr - KI
Cancerfonden	Rainer Heuchel	2009-01-01	2010-12-31	1265.000	Matthias Löhr - KI
EU	Carola Ponzetto	1998-01-01	2001-12-31	1500.000	C.-H. Heldin - LICR R. Heuchel - LICR
KI	Rainer Heuchel	2011-01-01	2011-12-01	100.000	Matthias Löhr - KI

### 8. Other merits:

2013- present	Member of the local ethical committee for animal experiments (Stockholms södra djurförsöksetiska nämnd)
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2012	Member of the External Science Advisory Board, CR-UK CCR, Liverpool, Great Britain
2010	Meeting Secretary of EMBO Workshop: Diseases, development and Stem Cells in the Pancreas

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Publication List, Rainer Heuchel

### ***1. Peer-reviewed original articles***

The publication list was prepared from a “PubMed” search.

Times cited information was received from “Web of Science”:

Sum of Times Cited without self-citations: 3554

h-index: 21

1 Schober M, Jesenofsky R, Faissner R, Weidenauer C, Haggmann W, et al. Desmoplasia and chemoresistance in pancreatic cancer. *Cancers (Basel)*. 2014 Oct 21;6(4):2137-54. PubMed PMID: 25337831; PubMed Central PMCID: PMC4276960. Number of citations: 0

2 Marschallinger J, Krampert M, Couillard-Despres S, Heuchel R, Bogdahn U, et al. Age-dependent and differential effects of Smad7 $\Delta$ Ex1 on neural progenitor cell proliferation and on neurogenesis. *Exp Gerontol*. 2014 Sep;57:149-54. PubMed PMID: 24862634; PubMed Central PMCID: PMC4162458. Number of citations: 1

3 Sjöqvist S, Jungebluth P, Lim ML, Haag JC, Gustafsson Y, et al. Experimental orthotopic transplantation of a tissueengineered oesophagus in rats. *Nat Commun*. 2014 Apr 15;5:3562. PubMed PMID: 24736316; PubMed Central PMCID: PMC4354271. Number of citations: 2

4 Gerling M, Zhao Y, Nania S, Norberg KJ, Verbeke CS, et al. Real-time assessment of tissue hypoxia in vivo with combined photoacoustics and high-frequency ultrasound. *Theranostics*. 2014;4(6):604-13. PubMed PMID: 24723982; PubMed Central PMCID: PMC3982131. Number of citations: 3

5 Estrada KD, Wang W, Retting KN, Chien CT, Elkhoury FF, et al. Smad7 regulates terminal maturation of chondrocytes in the growth plate. *Dev Biol*. 2013 Oct 15;382(2):375-84. PubMed PMID: 23994637; NIHMSID: NIHMS647309; PubMed Central PMCID: PMC4267888. Number of citations: 5

6 Wang J, Zhao J, Chu ES, Mok MT, Go MY, et al. Inhibitory role of Smad7 in hepatocarcinogenesis in mice and in vitro. *JPathol*. 2013 Aug;230(4):441-52. PubMed PMID: 23625826. Number of citations: 7

7 Longati P, Jia X, Eimer J, Wagman A, Witt MR, et al. 3D pancreatic carcinoma spheroids induce a matrix-rich, chemoresistant phenotype offering a better model for drug testing. *BMC Cancer*. 2013 Feb 27;13:95. PubMed PMID: 23446043; PubMed Central PMCID: PMC3617005. Number of citations: 17

8 Wei LH, Huang XR, Zhang Y, Li YQ, Chen HY, et al. Deficiency of Smad7 enhances cardiac remodeling induced by angiotensin II infusion in a mouse model of hypertension. *PLoS One*. 2013;8(7):e70195. PubMed PMID: 23894614; PubMed Central PMCID: PMC3720917. Number of citations: 0

- 9 Liu GX, Li YQ, Huang XR, Wei L, Chen HY, et al. Disruption of Smad7 promotes ANG II-mediated renal inflammation and fibrosis via Sp1-TGF- $\beta$ /Smad3-NF $\kappa$ B-dependent mechanisms in mice. *PLoS One*. 2013;8(1):e53573. PubMed PMID: 23301086; PubMed Central PMCID: PMC3536757. Number of citations: 12
- 10 Lonardo E, Hermann PC, Mueller MT, Huber S, Balic A, et al. Nodal/Activin signaling drives self-renewal and tumorigenicity of pancreatic cancer stem cells and provides a target for combined drug therapy. *Cell Stem Cell*. 2011 Nov 4;9(5):433-46. PubMed PMID: 22056140. Number of citations: 110
- 11 Dahal BK, Heuchel R, Pullamsetti SS, Wilhelm J, Ghofrani HA, et al. Hypoxic pulmonary hypertension in mice with constitutively active platelet-derived growth factor receptor- $\beta$ . *Pulm Circ*. 2011 Apr-Jun;1(2):259-68. PubMed PMID: 22034611; PubMed Central PMCID: PMC3198653.
- 12 Chen HY, Huang XR, Wang W, Li JH, Heuchel RL, et al. The protective role of Smad7 in diabetic kidney disease: mechanism and therapeutic potential. *Diabetes*. 2011 Feb;60(2):590-601. PubMed PMID: 20980457; PubMed Central PMCID: PMC3028360. Number of citations: 51
- 13 Pazirandeh A, Sultana T, Mirza M, Rozell B, Hultenby K, et al. Multiple phenotypes in adult mice following inactivation of the Coxsackievirus and Adenovirus Receptor (Car) gene. *PLoS One*. 2011;6(6):e20203. PubMed PMID: 21674029; PubMed Central PMCID: PMC3108585. Number of citations: 13
- 14 Shimokawa N, Haglund K, Hölter SM, Grabbe C, Kirkin V, et al. CIN85 regulates dopamine receptor endocytosis and governs behaviour in mice. *EMBO J*. 2010 Jul 21;29(14):2421-32. PubMed PMID: 20551902; PubMed Central PMCID: PMC2910270. Number of citations: 17
- 15 Krampert M, Chirasani SR, Wachs FP, Aigner R, Bogdahn U, et al. Smad7 regulates the adult neural stem/progenitor cell pool in a transforming growth factor beta- and bone morphogenetic protein-independent manner. *Mol Cell Biol*. 2010 Jul;30(14):3685-94. PubMed PMID: 20479122; PubMed Central PMCID: PMC2897544. Number of citations: 11
- 16 Lu N, Carracedo S, Ranta J, Heuchel R, Soininen R, et al. The human alpha11 integrin promoter drives fibroblast-restricted expression in vivo and is regulated by TGF-beta1 in a Smad- and Sp1-dependent manner. *Matrix Biol*. 2010 Apr;29(3):166-76. PubMed PMID: 19913614. Number of citations: 8
- 17 Chung AC, Huang XR, Zhou L, Heuchel R, Lai KN, et al. Disruption of the Smad7 gene promotes renal fibrosis and inflammation in unilateral ureteral obstruction (UUO) in mice. *Nephrol Dial Transplant*. 2009 May;24(5):1443-54. PubMed PMID: 19096081. Number of citations: 61
- 18 Krampert M, Heldin CH, Heuchel RL. A gain-of-function mutation in the PDGFR-beta alters the kinetics of injury response in liver and skin. *Lab Invest*. 2008 Nov;88(11):1204-14. PubMed PMID: 18762776. Number of citations: 5

- 19 Hamzavi J, Ehnert S, Godoy P, Ciuculan L, Weng H, et al. Disruption of the Smad7 gene enhances CCl4-dependent liver damage and fibrogenesis in mice. *J Cell Mol Med*. 2008 Oct;12(5B):2130-44. PubMed PMID: 18266971.  
Number of citations: 21
- 20 Suzuki S, Heldin CH, Heuchel RL. Platelet-derived growth factor receptor-beta, carrying the activating mutation D849N, accelerates the establishment of B16 melanoma. *BMC Cancer*. 2007 Dec 12;7:224. PubMed PMID: 18076756; PubMed Central PMCID: PMC2234427. Number of citations: 3
- 21 Weng HL, Ciuculan L, Liu Y, Hamzavi J, Godoy P, et al. Profibrogenic transforming growth factor-beta/activin receptorlike kinase 5 signaling via connective tissue growth factor expression in hepatocytes. *Hepatology*. 2007 Oct;46(4):1257-70. PubMed PMID: 17657819. Number of citations: 63
- 22 Magnusson PU, Looman C, Ahgren A, Wu Y, Claesson-Welsh L, et al. Platelet-derived growth factor receptor-beta constitutive activity promotes angiogenesis in vivo and in vitro. *Arterioscler Thromb Vasc Biol*. 2007 Oct;27(10):2142-9. PubMed PMID: 17656670. Number of citations: 27
- 23 Singh U, Sun T, Looman C, Heuchel R, Elliott R, et al. Expression and function of the gene encoding the voltage-dependent calcium channel beta3-subunit in the mouse placenta. *Placenta*. 2007 May-Jun;28(5-6):412-20. PubMed PMID: 16822546. Number of citations: 1
- 24 Looman C, Sun T, Yu Y, Zieba A, Ahgren A, et al. An activating mutation in the PDGF receptor-beta causes abnormal morphology in the mouse placenta. *Int J Dev Biol*. 2007;51(5):361-70. PubMed PMID: 17616925.  
Number of citations: 6
- 25 Rolny C, Nilsson I, Magnusson P, Armulik A, Jakobsson L, et al. Platelet-derived growth factor receptor-beta promotes early endothelial cell differentiation. *Blood*. 2006 Sep 15;108(6):1877-86. PubMed PMID: 16690964.  
Number of citations: 34
- 26 Li R, Rosendahl A, Brodin G, Cheng AM, Ahgren A, et al. Deletion of exon I of SMAD7 in mice results in altered B cell responses. *J Immunol*. 2006 Jun 1;176(11):6777-84. PubMed PMID: 16709837. Number of citations: 48
- 27 Lu N, Heuchel R, Barczyk M, Zhang WM, Gullberg D. Tandem Sp1/Sp3 sites together with an Ets-1 site cooperate to mediate alpha11 integrin chain expression in mesenchymal cells. *Matrix Biol*. 2006 Mar;25(2):118-29. PubMed PMID: 16300938.  
Number of citations: 15
- 28 Chiara F, Goumans MJ, Forsberg H, Ahgrén A, Rasola A, et al. A gain of function mutation in the activation loop of platelet-derived growth factor beta-receptor deregulates its kinase activity. *J Biol Chem*. 2004 Oct 8;279(41):42516-27. PubMed PMID: 15284236. Number of citations: 14



- 29 Furuhashi M, Sjöblom T, Abramsson A, Ellingsen J, Micke P, et al. Platelet-derived growth factor production by B16 melanoma cells leads to increased pericyte abundance in tumors and an associated increase in tumor growth rate. *Cancer Res.* 2004 Apr 15;64(8):2725-33. PubMed PMID: 15087386. Number of citations: 96
- 30 Pant V, Mariano P, Kanduri C, Mattsson A, Lobanenkova V, et al. The nucleotides responsible for the direct physical contact between the chromatin insulator protein CTCF and the H19 imprinting control region manifest parent of origin-specific long-distance insulation and methylation-free domains. *Genes Dev.* 2003 Mar 1;17(5):586-90. PubMed PMID:12629040; PubMed Central PMCID: PMC196004. Number of citations: 101
- 31 Edlund S, Bu S, Schuster N, Aspenström P, Heuchel R, et al. Transforming growth factor-beta1 (TGF-beta)-induced apoptosis of prostate cancer cells involves Smad7-dependent activation of p38 by TGF-beta-activated kinase 1 and mitogen-activated protein kinase kinase 3. *Mol Biol Cell.* 2003 Feb;14(2):529-44. PubMed PMID: 12589052; PubMed Central PMCID: PMC149990. Number of citations: 131
- 32 Arsur M, Panta GR, Bilyeu JD, Cavin LG, Sovak MA, et al. Transient activation of NF-kappaB through a TAK1/IKK kinase pathway by TGF-beta1 inhibits AP-1/SMAD signaling and apoptosis: implications in liver tumor formation. *Oncogene.* 2003 Jan 23;22(3):412-25. PubMed PMID: 12545162. Number of citations: 89
- 33 Tallquist MD, Klinghoffer RA, Heuchel R, Muetting-Nelsen PF, Corrin PD, et al. Retention of PDGFR-beta function in mice in the absence of phosphatidylinositol 3'-kinase and phospholipase C-gamma signaling pathways. *Genes Dev.* 2000 Dec 15;14(24):3179-90. PubMed PMID: 11124809; PubMed Central PMCID: PMC317125. Number of citations: 52
- 34 Brodin G, Ahgren A, ten Dijke P, Heldin CH, Heuchel R. Efficient TGF-beta induction of the Smad7 gene requires cooperation between AP-1, Sp1, and Smad proteins on the mouse Smad7 promoter. *J Biol Chem.* 2000 Sep 15;275(37):29023-30. PubMed PMID: 10843994. Number of citations: 110
- 35 Heuchel R, Berg A, Tallquist M, Ahlén K, Reed RK, et al. Platelet-derived growth factor beta receptor regulates interstitial fluid homeostasis through phosphatidylinositol-3' kinase signaling. *Proc Natl Acad Sci U S A.* 1999 Sep 28;96(20):11410-5. PubMed PMID: 10500190; PubMed Central PMCID: PMC18047. Number of citations: 130
- 36 Günes C, Heuchel R, Georgiev O, Müller KH, Lichtlen P, et al. Embryonic lethality and liver degeneration in mice lacking the metal-responsive transcriptional activator MTF-1. *EMBO J.* 1998 May 15;17(10):2846-54. PubMed PMID: 9582278; PubMed Central PMCID: PMC1170625. Number of citations: 187
- 37 Nakao A, Afrakhte M, Morén A, Nakayama T, Christian JL, et al. Identification of Smad7, a TGF-beta-inducible antagonist of TGF-beta signalling. *Nature.* 1997 Oct 9;389(6651):631-5. PubMed PMID: 9335507.

Number of citations: 1122

38 Wan M, Heuchel R, Radtke F, Hunziker PE, Kägi JH. Regulation of metallothionein gene expression in Cd- or Zn adapted RK-13 cells. *Experientia*. 1995 Jun 14;51(6):606-11. PubMed PMID: 7607305. Number of citations: 7

39 Brugnera E, Georgiev O, Radtke F, Heuchel R, Baker E, et al. Cloning, chromosomal mapping and characterization of the human metal-regulatory transcription factor MTF-1. *Nucleic Acids Res*. 1994 Aug 11;22(15):3167-73. PubMed PMID:8065932; PubMed Central PMCID: PMC310292. Number of citations: 143

40 Heuchel R, Radtke F, Georgiev O, Stark G, Aguet M, et al. The transcription factor MTF-1 is essential for basal and heavy metal-induced metallothionein gene expression. *EMBO J*. 1994 Jun 15;13(12):2870-5. PubMed PMID: 8026472; PubMed Central PMCID: PMC395168. Number of citations: 324

41 Radtke F, Heuchel R, Georgiev O, Hergersberg M, Gariglio M, et al. Cloned transcription factor MTF-1 activates the mouse metallothionein I promoter. *EMBO J*. 1993 Apr;12(4):1355-62. PubMed PMID: 8467794; PubMed Central PMCID: PMC413347. Number of citations: 293

42 Zeng J, Heuchel R, Schaffner W, Kägi JH. Thionein (apometallothionein) can modulate DNA binding and transcription activation by zinc finger containing factor Sp1. *FEBS Lett*. 1991 Feb 25;279(2):310-2. PubMed PMID: 2001744. Number of citations: 240

43 Heuchel R, Matthias P, Schaffner W. Two closely spaced promoters are equally activated by a remote enhancer: evidence against a scanning model for enhancer action. *Nucleic Acids Res*. 1989 Nov 25;17(22):8931-47. PubMed PMID:2555780; PubMed Central PMCID: PMC335104. Number of citations: 17

44 Leist TP, Heuchel R, Zinkernagel RM. Increased bactericidal macrophage activity induced by immunological stimuli is dependent on interferon (IFN)-gamma. Interference of anti-IFN-gamma but not anti-IFN-alpha/beta with modulation of macrophage activity caused by lymphocytic choriomeningitis virus infection or systemic graft-vs-host reactions. *Eur J Immunol*. 1988 Aug;18(8):1295-8. PubMed PMID: 3138138. Number of citations: 15

#### **4. Review articles**

1. Schober M, Jesenofsky R, Faissner R, Weidenhauer C, Hagmann W, Neesse A, Michl P, **Heuchel RL**, Haas SL, Löhr JM (2014): Desmoplasia and chemoresistance in pancreatic cancer. **Cancers**, 6: 2137-2154.

2. Löhr JM, **Heuchel R**, Jesnowski R, Wallrapp C (2009): Therapy with Cell Encapsulation for Substitution of Organ Function and Tumor Treatment. **Advanced Engineering Materials** 11: B129-B135.

### ***5. Book Chapters***

1. Löhr M, Haas SL, **Heuchel R** (2011): Pathophysiology of pancreatic cancer. In: **Advances in Pancreatic cancer**. Friess H (Ed). E-book. eISBN (PDF): 978-1-78084-070-3