BIOGRAPHICAL SKETCH

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NAME: KAARTINEN, VESA M

eRA COMMONS USER NAME (credential, e.g., agency login): VKAARTINEN

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
University of Eastern Finland-Kuopio, Kuopio	BS	03/1984	Biochemistry
University of Eastern Finland-Kuopio, Kuopio	MS	04/1986	Biochemistry
University of Eastern Finland-Kuopio, Kuopio	PHD	08/1991	Biochemistry and Molecular Biology
Children's Hospital Los Angeles and Keck School of Medicine, University of Southern California, Los Angeles, CA	Postdoctoral Fellow	12/1996	Molecular Biology & Mouse Genetics

A. Personal Statement

My research program focuses on that regulate cardiac and craniofacial development. Failure in these processes results in common birth defects, such as congenital cardiac malformations and cleft palate. I have more than 30 years of experience in biochemistry, molecular biology and mouse genetics. We extensively use genetically manipulated mouse models to examine mechanisms, which are critically important for appropriate mammalian embryogenesis.

B. Positions and Honors

Positions and Employment

1997 - 2004	Asst. Professor of Research, Children's Hospital Los Angeles & Keck School of Medicine, University of Southern California, Department of Pathology, Los Angeles, CA
2004 - 2008	Assistant Professor (tenure track), Children's Hospital Los Angeles & Keck School of Medicine, University of Southern California, Departments of Pathology and Surgery, Los Angeles, CA
2008 - 2014	Associate Professor, University of Michigan, School of Dentistry - Biologic & Materials Sciences, Ann Arbor, MI
2014 -	Professor, University of Michigan, School of Dentistry - Biologic & Materials Sciences, Ann Arbor, MI
2018 -	Director, OHS PhD program, University of Michigan School of Dentistry, Ann , MI
2019 -	Associate Dean for Research, University of Michigan School of Dentistry, Ann Arbor, MI
2020 -	Roy H. Roberts Professor, University of Michigan School of Dentistry, Ann Arbor, MI

Other Experience and Professional Memberships

2001 - 2002	Grant Reviewer, Action Research (UK)
2002 - 2002	Ad Hoc Member, NIDCR NIH Special Emphasis Panel Review for RFA (Gene Discovery for Craniofacial Disorders)
2002 - 2017	Ad Hoc Reviewer, Nature genetics, NEJM, Dev Cell, Development, Dev Biol, Dev Dyn, Mol Cell Biol, PlosOne, PlosBiol, PlosGenet, Lancet, J Biol Chem, Stem Cell & Dev.
2003 - 2003	Grant Reviewer, Breakthrough Breast Cancer (UK)
2004 - 2004	Ad Hoc Member, NIH Study Section, Development 2

2004 - 2004	Ad Hoc Member, NICHD NIH Special Emphasis Panel Review for RFA (Comparative Genetics of Structural Birth Defects)
2004 - 2004	Grant Reviewer, Telethon (Italy)
2006 - 2006	Ad Hoc Member, NIDCR Special Grants Review Committee
2006 - 2006	Ad Hoc Member, NIH Study Section, ZRG1 BDA-F (02)
2006 - 2010	Member, Peer Review Committee 3A, American Heart Association, Western Review Consortium.
2007 - 2007	Ad Hoc Member, NIH Study Section, NHLBI Signaling networks Valve – PPG Workgroup.
2009 - 2012	Editorial Board Member, Journal of Dental Research
2010 -	Member, CVD2 review group, American Heart Association
2010 - 2017	Associate Editor, Frontiers in Physiology- Craniofacial Biology.
2011 - 2011	Ad Hoc Member, NIDCR Special Grants Review Committee
2011 - 2011	Ad Hoc Member, NIH Study Section, Cardiovascular Differentiation and Development (CDD)
2011 - 2011	Ad Hoc Member, NIDCR Special Grants Review Committee
2011 - 2011	Ad Hoc Member, NIH Study Section, Cardiovascular Differentiation and Development (CDD).
2011 - 2015	Academic Editor, PlosOne
2011 - 2017	Editorial Board Member, Developmental Biology
2012 - 2012	Ad Hoc Member, NIH Study Section, ZRG1 CVRS-M (02).
2012 - 2012	Ad Hoc Member, NIH Study Section, ZRG1 CVRS-N (02)
2014 - 2014	Ad Hoc Member, NIH Study Section ZRG1 CVRS-E (02) M
2014 - 2014	Ad Hoc Member, NIH Study Section ZRG1 Moss DO2
2014 - 2017	Editorial Board Member, Scientific Reports
2017 - 2017	Ad Hoc Member, NIH Study Section, Cardiovascular Differentiation and Development (CDD)
2018 - 2018	Ad Hoc Member, NIH Study Section ZDE1 CF17 LRP
2019 - 2019	Chair, NIH Study Section ZDE1 YM (16)
2020 - 2020	Ad Hoc Member, NIH Study Section ZDE1 YM (22)
2020 - 2020	Ad Hoc Member, NIH Study Section ZDE1 YM05

Honors

1991	Emanuel Merck Award, Finnish Chemical Society
1996	Junior Fellow, The Finnish Academy of Science, Finland
1998	Research Career Development Award, Children's Hospital Los Angeles
2006	Docent, Developmental Biochemistry, University of Eastern Finland-Kuopio, Finland
2006	H. Russell Smith award for innovation in Pediatric Biomedical Research, Children's Hospital Los Angeles
2013	Sulo Toivonen keynote lecture & medal, The Finnish Society for Developmental Biology

C. Contribution to Science

1. My early work presents groundbreaking studies in purification of the glycosylasparaginase enzyme and cloning its gene, which is deficient in a fatal metabolic disease aspartylglycosaminuria. These papers also describe analysis of a reaction mechanism of glycosylasparaginase and present a mouse model for aspartylglycosaminuria, which I generated using gene targeting in embryonic stem cells. I served as the primary investigator or co-investigator in all of these studies.

    a. Kaartinen V, Williams JC, Tomich J, Yates JR 3rd, Hood LE, Mononen I. Glycosaparaginase from human leukocytes. Inactivation and covalent modification with diazo-oxonorvaline. J Biol Chem. 1991 Mar 25;266(9):5860-9. PubMed PMID: 2005122.

    b. Mononen I, Heisterkamp N, Kaartinen V, Mononen T, Williams JC, Groffen J. Aspartylglycosaminuria in a non-Finnish patient caused by a donor splice mutation in the glycoasparaginase gene. J Biol Chem. 1992 Feb 15;267(5):3196-9. PubMed PMID: 1737774.

c. Kaartinen V, Mononen T, Laatikainen R, Mononen I. Substrate specificity and reaction mechanism of human glycoasparaginase. The N-glycosidic linkage of various glycoasparagines is cleaved through a reaction mechanism similar to L-asparaginase. J Biol Chem. 1992 Apr 5;267(10):6855-8. PubMed PMID: 1551892.

d. Kaartinen V, Mononen I, Voncken JW, Noronkoski T, Gonzalez-Gomez I, Heisterkamp N, Groffen J. A mouse model for the human lysosomal disease aspartylglycosaminuria. Nat Med. 1996 Dec;2(12):1375-8. PubMed PMID: 8946839.

2. In vivo studies on the TGF-beta3 ligand provoked my interest in TGF-beta receptor signaling. To this end I generated a conditional allele for a somewhat atypical Type-I receptor (Acvr1/Alk2), of which signaling characteristics, particularly in vivo, were at the time poorly known. We discovered that this receptor plays an important role in craniofacial neural crest cells by controlling cell proliferation. Subsequent studies have shown that mutations in this gene are responsible for the devastating FOP disease resulting in ectopic ossifications. Our subsequent studies have concentrated in canonical and non-canonical TGF-beta signaling processes in neural crest pathology. These studies highlight the critical role TGF-beta signaling plays in differentiation of neural crest-derived ectomesenchyme,and therefore they have contributed in understanding of molecular bases of TGF-beta superfamily signaling in pathogenetic mechanisms of craniofacial birth defects.

   a. Lees-Shepard JB, Yamamoto M, Biswas AA, Stoessel SJ, Nicholas SE, Cogswell CA, Devarakonda PM, Schneider MJ Jr, Cummins SM, Legendre NP, Yamamoto S, Kaartinen V, Hunter JW, Goldhamer DJ. Activin-dependent signaling in fibro/adipogenic progenitors causes fibrodysplasia ossificans progressiva. Nat Commun. 2018 Feb 2;9(1):471. PubMed PMID: 29396429; PubMed Central PMCID: PMC5797136.

   b. Yumoto K, Thomas PS, Lane J, Matsuzaki K, Inagaki M, Ninomiya-Tsuji J, Scott GJ, Ray MK, Ishii M, Maxson R, Mishina Y, Kaartinen V. TGF-β-activated kinase 1 (Tak1) mediates agonist-induced Smad activation and linker region phosphorylation in embryonic craniofacial neural crest-derived cells. J Biol Chem. 2013 May 10;288(19):13467-80. PubMed PMID: 23546880; PubMed Central PMCID: PMC3650384.

   c. Dudas M, Kim J, Li WY, Nagy A, Larsson J, Karlsson S, Chai Y, Kaartinen V. Epithelial and ectomesenchymal role of the type I TGF-beta receptor ALK5 during facial morphogenesis and palatal fusion. Dev Biol. 2006 Aug 15;296(2):298-314. PubMed PMID: 16806156; PubMed Central PMCID: PMC1557652.

   d. Dudas M, Sridurongrit S, Nagy A, Okazaki K, Kaartinen V. Craniofacial defects in mice lacking BMP type I receptor Alk2 in neural crest cells. Mech Dev. 2004 Feb;121(2):173-82. PubMed PMID: 15037318.

3. Our studies on TGF-beta superfamily signaling in neural crest-derived cells demonstrated that these signaling processes are not important only in craniofacial development, but also in cardiac morphogenesis. These studies lead to several significant discoveries on the role of TGF-beta superfamily signaling in cardiac outflow tract septation, outflow tract and atrio-ventricular valve development and myocardial differentiation. Results of these studies are significant, since they have helped in understanding of molecular mechanisms controlling appropriate cardiac morphogenesis failure of which results in the most common lethal congenital birth defects in humans.

   a. Rajderkar S, Mann JM, Panaretos C, Yumoto K, Li HD, Mishina Y, Ralston B, Kaartinen V. Trim33 is required for appropriate development of pre-cardiogenic mesoderm. Dev Biol. 2019 Jun 15;450(2):101-114. PubMed PMID: 30940539; PubMed Central PMCID: PMC6547372.

   b. Thomas PS, Rajderkar S, Lane J, Mishina Y, Kaartinen V. AcvR1-mediated BMP signaling in second heart field is required for arterial pole development: implications for myocardial differentiation and regional identity. Dev Biol. 2014 Jun 15;390(2):191-207. PubMed PMID: 24680892; PubMed Central PMCID: PMC4057048.

   c. Wang J, Sridurongrit S, Dudas M, Thomas P, Nagy A, Schneider MD, Epstein JA, Kaartinen V. Atrioventricular cushion transformation is mediated by ALK2 in the developing mouse heart. Dev Biol. 2005 Oct 1;286(1):299-310. PubMed PMID: 16140292; PubMed Central PMCID: PMC1361261.

d. Kaartinen V, Dudas M, Nagy A, Sridurongrit S, Lu MM, Epstein JA. Cardiac outflow tract defects in mice lacking ALK2 in neural crest cells. Development. 2004 Jul;131(14):3481-90. PubMed PMID: 15226263.

4. Our studies on TGF-beta3 have revealed that this ligand, which is specifically expressed in epithelial tips of prefusion palatal shelves, is critically important for appropriate palate fusion. It functions both in the periderm to regulate adhesion, and in the underlying epithelial cells to mediate epithelial fusion. Our subsequent studies have shown that some of these functions are isoform-specific. Moreover, we have identified putative palate-specific enhancers and unravelled signaling mechanisms triggered by TGF-beta3 during palatal epithelial fusion. Results of these studies are significant, since they have helped to unravel the pathogenetic mechanisms behind the cleft palate syndrome, one of the most common birth defects in humans.

Complete List of Published Work in My Bibliography (114 total):
https://www.ncbi.nlm.nih.gov/myncbi/vesa.kaartinen.1/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

5K12DE027826-02, NIH/NIDCR
KAARTINEN, VESA M (PI)
09/03/18-08/31/23
Accelerating interventions for craniofacial diseases and disorders via DSPP scholar training at Michigan
Role: PI

1RO3HD100602-01, NIH/NICHD
KAARTINEN, VESA M (PI)
02/20/20-01/31/22
DEVELOPMENT OF PERIDERM-SPECIFIC CRE MOUSE LINES TO STUDY PALATOGENESIS
Cleft palate is among the most common congenital birth defects in humans. We propose studies to explore mechanisms of periderm degeneration, which is required for appropriate palatal adhesion and fusion. The proposed experiments are likely to be of critical importance in attempting to understand the molecular basis of the cleft palate syndrome in humans and in development of strategies to prevent and treat this malformation.
Role: PI

Completed Research Support

1R56DE026464-01A1, National Institute of Dental & Craniofacial Research (NIDCR)
KAARTINEN, VESA M (PI)
09/05/17-09/04/19
TGFbeta 3 signaling in palatal periderm degeneration
The objective of this grant is to unravel the role of TGFbeta3 signaling in palatal periderm degeneration.
Role: CPI