Education - Positions

Education:

1978-1984	Technical University Darmstadt, Germany, study of Chemistry
1983	Diploma (final examination)
1983-1984	Preparation of diploma thesis “Identification of α-chains of collagen I in gelatine” (supervisor: Prof. E. Heidemann) Institute of Macromolecular Chemistry, Department of Protein Chemistry, Darmstadt
1985-1988	Preparation of doctoral thesis “Interaction of Progesterone- and Glucocorticoid-Receptor with the regulatory elements of the Mouse Mammary Tumor Virus (MMTV)” (supervisor: Prof. M. Beato) Institute of Molecular Biology and Tumor Research, Marburg, Germany
1988	Doctorate, Marburg University
1988-1990	Postdoctoral assistant at the Institute of Molecular Biology and Tumor Research, Marburg, Germany Research field: Gene regulation by steroid hormone receptors
1990-1991	Postdoctoral fellow (Stipend of Boehringer-Ingelheim), Max-Planck-Institute of Biophysical Chemistry, Goettingen, Germany Department of Molecular Cell biology in the group of Prof. P. Gruss
1991-1996	Senior scientist in Max-Planck-Institute of Biophysical Chemistry, Goettingen Research topics: Functional analysis of Pax-gene products and identification of neuronal specific genes using the gene-trap method in mouse

Positions:

1996-2008	Associate Prof. of Cell Biology at the Department of Biology, University of Crete
2009	Professor of Cell Biology at the Department of Biology, University of Crete.

Research Interests

During his career Dr. Chalepakis has been involved in different projects including functional characterization of gene products as well as developmental genetics using gene manipulation techniques in mouse. His major interest over the time between 1990 and 1996 was to elucidate the molecular and cellular function of proteins (Pax-proteins) which have been associated with mouse mutants and human syndromes (mouse mutants: undulated, splotch, small eye; Human syndromes: Waardenburg, Aniridia). Dr. Chalepakis has also been involved in a large scale gene trap project in the Group of Prof. Peter Gruss at the Max-Planck-Institute in Goettingen (Germany) with the aim to create as many random mutations in the mouse genome as possible. In September 1996, Dr. Chalepakis took his present position at the University of Crete. His group has isolated and characterized the *Fras1* gene in mouse and in collaboration with Dr. P. Scambler (UK) have shown that mutations in the human counterpart *FRAS1,* are responsible for the Fraser syndrome. Fraser syndrome is a rare genetic disorder with autosomal recessive inheritance pattern, primarily characterized by cryptophthalmos, syndactyly and renal agenesis. The group of Dr. Chalepakis has generated the *Fras1* deficient mice which serve as model to investigate the molecular pathology of the human Fraser syndrome. In addition to Fras1, the family of Fras1/Frem proteins comprises three additional members, Frem1, Frem2 and Frem3 which interact with each other to form an interdependent macromolecular protein complex within the basement membrane surrounding the embryonic epithelia. The major focus of the research group is to identify the proteins which interact with Fras1/Frem, aiming to explore the composition, the assembly and the protein-protein interactions of the extracellular matrix components that underlie epithelia and confer the structural cohesiveness as well as the functional interaction between epithelia and mesenchyme in mammals.

Other Scientific Responsibilities

Dr. Chalepakis is the director of the laboratory of Electron Microscopy 'Vassilis Galanopoulos' which belongs to the Faculty of Sciences and Technology of the University of Crete. The facility offers its services not only to the scientific community of the University of Crete but to the whole of Greece. The activities of the laboratory are not confined only to basic research, as electron microscopy is a useful tool for dermatologists, ophthalmologists and nephrologists for the diagnosis of specific pathologies.

The laboratory is well equipped with two Transmission Electron Microscopes (TEM), a JEOL-100C and a high resolution JEM-2100 microscope (which provide solutions for a wide range of problems in the fields of materials, nanoelectronics and biological sciences). Two Scanning Electron Microscopes, a JSM 840 and a JSM-6390LV complement the facility of electron microscopy. In addition, the laboratory is equipped with a low energy ion milling for sample

preparation for nanoanalytical electron microscopy, a sputtering SCD 050 sample coater for SEM, a critical point dryer CPD 030, a cryo-preparation Leica EM AFS, an ultramicrotome LKB 2088 and knife maker LKB 7800B. Furthermore, the facility is equipped with a confocal Microscope SP1 LEICA, an optical microscope NIKON eclipse E800 and an Axiovert D1 Time-lapse microscopy system. The microscopes are fully equipped for routine activities such as simple observation of biological tissue preparations and nanomaterials.

PUBLICATIONS

Pavlakis, E., Chiotaki, R. and Chalepakis, G. (2011). The role of Fras1/Frem proteins in the structure and function of basement membrane. **Int. J. Biochem. Cell Biol.** 43, 487-495.

Pavlakis, E., Makrygiannis, A., Chiotakis, R. and Chalepakis, G. (2008). Differential localization profile of Fras1/Frem proteins in epithelial basement membranes of newborn and adult mice. **Histochem. Cell. Biol.** 130, 785-793.

Petrou, P., Makrygiannis, A. and Chalepakis, G. (2008). The Fras1/Frem family of extracellular matrix proteins: Structure, function and association with Fraser syndrome and the mouse bleb phenotype. **Connect. Tissue Res.** 49, 277-282.

Pavlakis, E. and Chalepakis, G. (2008). pH-dependent antigen unmasking in paraformaldehyde-fixed tissue cryosections. **Appl. Immunohistochem. Mol. Morphol.** 16, 503-506.

Dalezios, Y., Papasozomenos, B., Petrou, P. and Chalepakis G. (2007). Ultrastructural localization of Fras1 in the sublamina densa of embryonic epithelial basement membranes. **Arch. Dermatol. Res**. 299, 337-343.

Petrou, P., Pavlakis, E., Dalezios, Y. and Chalepakis, G. (2007). Basement membrane localization of Frem3 is independent of the Fras1/Frem1/Frem2 protein complex within the sublamina densa. **Matrix Biol**. 26, 652-658.

Petrou, P., Chiotaki, R., Dalezios, Y. and Chalepakis, G. (2007). Overlapping and divergent localization of Frem1 and Fras1 and its functional implications during mouse embryonic development. **Exp. Cell Res**. 313, 910-920.

Chiotaki, R., Petrou, P., Giakoumaki, E., Pavlakis, E., Sitaru, C. and Chalepakis, G. (2007). Spatiotemporal distribution of Fras1/Frem proteins during mouse embryonic development. **Gene Expression Patterns** 7, 381-388.

Jadeja, S., Smyth, I., Pitera, J.E., Taylor, M.S., van Haelst, M., Bentley, E., McGregor, L., Hopkins, J., Chalepakis, G., Philip, N., Perez Aytes, A., Watt, F.M., Darling, S.M., Jackson, I.,

Woolf, A.S. and Scambler, P.J. (2005). Identification of a new gene mutated in Fraser syndrome and mouse myelencephalic blebs. **Nat. Genet**. 37, 520-525.

Petrou, P., Pavlakis, E., Dalezios, Y., Galanopoulos, V.K. and Chalepakis, G. (2005). Basement membrane distortions impair lung lobation and capillary organization in the mouse model for Fraser syndrome. **J. Biol. Chem**. 280, 10350-10356.

Takamiya, K., Kostourou, V., Adams, S., Jadeja, S., Chalepakis, G., Scambler, P.J., Huganir, R.L. and Adams, R.H. (2004). A direct functional link between the multi-PDZ domain protein GRIP1 and the Fraser syndrome protein Fras1. **Nat. Genet**. 36, 172-177.

McGregor, L., Makela, V., Darling, S.M., Vrontou, S., Chalepakis, G., Roberts, C., Smart, N., Rutland, P., Prescott, N., Hopkins, J., Bentley, E., Shaw, A., Roberts, E., Mueller, R., Jadeja, S., Philip, N., Nelson, J., Francannet, C., Perez-Aytes, A., Megarbane, A., Kerr, B., Wainwright, B., Woolf, A.S., Winter, R.M. and Scambler, P.J. (2003). Fraser syndrome and mouse blebbed phenotype caused by mutations in FRAS1/Fras1 encoding a putative extracellular matrix protein. **Nat. Genet**. 34, 203-208.

Vrontou, S., Petrou, P., Meyer, B.I., Galanopoulos, V.K., Imai, K., Yanagi, M., Chowdhury, K., Scambler, P.J. and Chalepakis, G. (2003). Fras1 deficiency results in cryptophthalmos, renal agenesis and bleb phenotype in mice. **Nat. Genet**. 34, 209-214.

Papoutsopoulou, S., Nikolakaki, E., Chalepakis, G., Kruft, V., Chevaillier, P. and Giannakouros, T. (1999). SR protein-specific kinase 1 is highly expressed in testis and phosphorylates protamine 1. **Nucl. Acids Res**. 27, 2972-2980.

Song, D-Li, Chalepakis, G., Gruss, P. and Joyner, A.L. (1996). Two Pax-binding sites are required for early embryonic brain expression of an Engrailed-2 transgene. **Development** 122, 627-635.

Chalepakis, G. and Gruss, P (1995). Identification of DNA recognition sequences for the Pax3 paired domain. **Gene** 162, 267-270.

Chalepakis, G., Jones, F.S., Edelman, G.M. and Gruss, P. (1994). Pax-3 contains domains for transcription activation and transcription inhibition. **Proc. Natl. Acad. Sci. USA** 91, 12745-12749.

Chalepakis, G., Wijnholds, J. and Gruss, P. (1994). Pax-3 - DNA interaction: flexibility in the DNA binding and induction of DNA conformational changes by paired domains. **Nucl. Acids Res**. 22, 3131-3137.

Chalepakis, G., Wijnholds, J., Giese, P., Schachner, M. and Gruss, P. (1994). Characterization of Pax-6 and Hoxa-1 binding to the promoter region of the neural cell adhesion molecule L1. **DNA Cell. Biol**. 13, 891-900.

Chalepakis, G., Goulding, M., Read, A., Strachan, T. and Gruss, P. (1994). The molecular basis of splotch and Waardenburg Pax-3 mutations. **Proc. Natl. Acad. Sci. USA** 91, 3685-3689.

Chalepakis, G., Stoykova, A., Wijnholds, J., Tremblay, P. and Gruss, P. (1993). Pax: gene regulators in the developing nervous system. **J. Neurobiol**. 24, 1367-1384.

Fickenscher, H.R., Chalepakis, G. and Gruss, P. (1993). Murine Pax-2 protein is a sequence-specific trans-activator with expression in the genital system. **DNA Cell. Biol**. 12, 381-391.

Truss, M., Chalepakis, G. and Beato, M. (1992). Interplay of steroid hormone receptors and transcription factors on the mouse mammary tumor virus promoter. **J. Steroid Biochem. Mol. Biol**. 43, 365-378.

Chalepakis, G., Tremblay, P. and Gruss, P. (1992). Pax genes, mutants and molecular function. **J. Cell Sci**. 16 (Suppl.), 61-76.

Truss, M., Chalepakis, G., Pina, B., Barettino, D., Bruggemeier, U., Kalff, M., Slater, E.P. and Beato, M. Transcriptional control by steroid hormones. Review (1992). **J. Steroid Biochem. Mol. Biol**. 41, 241-248.

Truss, M., Bartsch, J., Chalepakis, G. and Beato, M. (1992). Artificial steroid hormone response element generated by dam-methylation. **Nucl. Acids Res**. 20, 1483-1486.

Jones, F.S., Chalepakis, G., Gruss, P. and Edelman G.M. (1992). Activation of the cytotactin promoter by the homeobox-containing gene Evx-1. **Proc. Natl. Acad. Sci. USA** 89, 2091-2095.

Chalepakis, G., Fritsch, R., Deutsch, U., Fickenscher, H., Goulding, M. and Gruss, P. (1991). The molecular basis of the undulated / Pax-1 muattion. **Cell** 66, 873-884.

Truss, M.*, Chalepakis, G.*, Slater, E.P., Mader, S. and Beato, M. (1991). Functional interaction of hybrid response elements with wild-type and mutant steroid hormone receptors. **Mol. Cell. Biol**. 11, 3247-3258.
* equal first authors

Goulding, M.D., Chalepakis, G., Deutsch, U., Erselius, J.R. and Gruss, P. (1991). Pax-3, a novel murine DNA binding protein expressed during early neurogenesis. **EMBO J**. 10, 1135-1147.

Pina, B., Hache, R.J.G., Arnemann, J., Chalepakis, G., Slater, E.P. and Beato, M. (1990). Hormonal induction of transfected genes depends on DNA topology. **Mol. Cell. Biol**. 10, 625-633.

Beato, M., Chalepakis, G., Schauer, M. and Slater, E. (1989). DNA regulatory elements for steroid hormones. **J. Steroid Biochem**. 32, 737-748.

Truss, M., Chalepakis, G. and Beato, M. (1989). Contacts between steroid hormone receptors and thymines in DNA: An interference method. **Proc. Natl. Acad. Sci. USA** 87, 7180-7184.

Chalepakis, G., Schauer, M., Cao, X.A. and Beato, M. (1989). Efficient binding of the glucocorticoid receptor to its responsive element requires two monomers and DNA flanking sequences. **DNA Cell. Biol**. 9, 355-368.

Slater, M.P., Posseckert, G., Chalepakis, G., Redeuihl, G. and Beato, M. (1989). Binding of steroid hormone receptors to the HREs of mouse mammary tumor virus, chicken and xenopus vitellogenin and rabbit uteroglobin genes: correlation with induction. **J. Steroid Biochem**. 34, 11-16.

Schauer, M., Chalepakis, G., Willmann, T. and Beato, M. (1989). Binding of hormone accelerates the kinetics of glucocorticoid and progesterone receptor binding to DNA. **Proc. Natl. Acad. Sci. USA** 86, 1123-1127.

Chalepakis, G. and Beato, M. (1989). Hydroxyl radical interference: a new method for the study of protein-DNA interactions. **Nucl. Acids Res**. 17, 1783.

Chalepakis, G., Postma, J.P.M. and Beato, M. (1988). A model for hormone receptor binding to the mouse mammary tumor virus regulatory element based on hydroxyl radical footprinting. **Nucl. Acids Res**. 16, 10237-10247.

Chalepakis, G., Arnemann, J., Slater, E., Bruller, H.-J., Gross, B. and Beato, M. (1988). Differential gene activation by glucocorticoids and progestins through the hormone regulatory element of mouse mammary tumor virus. **Cell** 53, 371- 382.

Beato, M., Arnemann, J., Chalepakis, G., Slater, E. and Willmann, T. (1987). Gene regulation by steroid hormones. **J. Steroid Biochem**. 27, 9-14.

Chalepakis, G., Tanay, I. and Heidemann, E. (1985). Wie spezifisch ist der Kollagenabbau bei der Gelatineherstellung? **Das Leder** 36, 2-10.

CHAPTERS IN BOOKS

Chalepakis, G. and Gruss, P. (1995). The Pax family of transcription factors in embryonic development. In "Organization of the early vertebrate embryo" (ed N. Zagris), Plenum Press, New York, 263-273.

Beato, M., Barettino, D., Bruggemeier, U., Chalepakis, G., Kalff, M., Pina, B. and Truss, M. (1991). Transcriptional regulation by steroid hormones. In "The Therapeutic Implications of the Molecular Biology of Breast Cancer" (ed E. Mihich) John Libbey CIC., 95-105.

Beato, M., Barettino, D., Bruggemeier, U., Chalepakis, G., Hache, R.J.G., Kalff, M., Pina, B., Schauer, M., Slater, E.P. and Truss, M. (1991). Characterization of DNA receptor interactions. In "Nuclear hormone receptors" (ed. M. Parker) Academic Press, 197-216.

Beato, M., Barettino, D., Bruggemeier, U., Chalepakis, G., Hache, R.J.G., Kalff, M., Pina, B., Slater, E.P. and Truss, M. (1991). Regulation of transcription by glucocorticoids. In "The Hormonal Control of Gene Expression" (ed. P. Cohen & J. G. Foulkes) Elsevier, 117-128.

Slater, E.P., Truss, M., Chalepakis, G. and Beato, M. (1990). A comparison of the binding sites for estrogen and progesterone receptors. In "Hormones and Cell Regulation" (Ed. J. E. Dumont, J. Nunez, & R. J. B. King) John Libbey Eurotext Ltd. 210, 103-113.

Chalepakis, G., Schauer, M., Slater, E.P. and Beato, M. (1990). Gene regulation by steroid hormones. In "Activation of hormone and growth factor receptors" (ed M. N. Alexis & C. E. Sekeris) Kluwer Acad Publ, 151-172.

Beato, M., Bruggemeier, U., Chalepakis, G., Gross, B., Pina, B., Schauer, M., Slater, E.P. and Truss, M. (1989). Interaction of steroid hormone receptors with DNA. in "Molecular Mechanisms of Hormone Action" (ed U. Gehring, E. Helmmreich & G. Schultz) Springer Verlag, 12-20.

Beato, M., Bruggemeier, U., Chalepakis, G., Schauer, M., Slater, E. and Willmann, T. (1988). Differential interaction of the receptors for glucocorticoids and progestins with the hormone regulatory element of MMTV. In "Nucl. Acids and Molecular Biology" (ed F. Eckstein & D. M. J. Liley) Springer-Verlag Vol. 2, 206-219.

Arnemann, J., Bruggemeier, U., Carballo, M., Chalepakis, G., Gross, B., Espel, E., Mugele, K., Pina, B., Posseckert, G., Slater, E., Willmann, T. and Beato, M. (1988). Differential gene regulation by steroid hormones. In "Steroid Hormone Action" (ed G. Ringlold) Alan R. Liss Inc., 185-192.