Christopher Konialis, M.Sc., Ph.D.

Clinical Molecular Geneticist

Born in Athens, Greece, in 1953, is a high school graduate of Athens College. Studied Chemistry at the University of Thessaloniki and immediately after moved to London UK, at University College London (UCL) for seven years, where he first obtained an MSc degree in Biochemistry and subsequently a PhD degree in Molecular Genetics on human gene cloning and expression.
During this period he also supervised laboratory courses for undergraduate students and was subsequently employed as a post-doctoral research fellow, working on an externally funded research project involving cloning, transfection and expression of human genes using retroviral vectors.

His work abroad was interrupted in 1985 in order to return to Greece for his army service and he remained in the country, employed as a Research Associate-Group Leader in the Center for Biological Research of the Hellenic Research Foundation, as head of a research group-project studying gene expression during differentiation and development of the human erythropoietic system.

After 5 years, he decided to move to the private sector, in the field of laboratory diagnostics, where the most notable achievement was his pioneering work on DNA Profiling technology and the establishment of the Forensic DNA Laboratory of the Greek police in 1994.

During the last 15 years he is at InterGenetics SA - Diagnostic Genetics Centre, as Head of The Department of Molecular Genetics and Genomics and of the Prenatal Biochemical Testing Unit.

In late 2011-early 2012 he established the Next Generation Sequencing facility at InterGenetics, and since he has been personally and primarily involved in the clinical interpretation of NGS data and the diagnosis of several hundred patient cases investigated primarily through Whole Exome Sequencing studies, including cutting-edge pioneering applications of exome sequencing in fetuses with ultrasound abnormalities.

During the last 5 years he developed, in close collaboration with Prof. Z. Agioutantis, currently Mining Engineering Foundation Professor at the University of Kentucky, a cutting-edge bioinformatics pipeline for variant prioritization and clinical interpretation of NGS data. In late 2016 he founded ClinGenics (UK) Ltd, a company based in London, UK, with the aim of commercializing the phenotype-driven bioinformatics software pipeline, *Exome Management Application-EMA®*, together with other closely related medical genomics bioinformatics tools (e.g. *NGS-PanelBuilder®*) and also aiming to provide comprehensive clinical genomic testing solutions.

Overall, has more than 30 years of experience in molecular genetics and clinical molecular genetics and genomics. Is a member of various international scientific societies (ASHG, ESHG, BSGM, ESHRE and others), has published many first-author original papers in international journals and he actively participates as a speaker in many national and international meetings and congresses in the field of medical genetics and genomics.

CURRICULUM VITAE

Christopher P. Konialis, MSc, PhD
Clinical Molecular Geneticist

BORN: November 18, 1953, Athens, Greece

Prepared: February 1, 2018

CURRENT POSITIONS

Founder and Director, ClinGenics (UK) Ltd
15 Hanover Square
London W1S 1HS
United Kingdom
www.clingenics.co.uk

Head of the Department of Molecular Genetics and Genomics
Head of the Prenatal Biochemical Screening Unit
InterGenetics SA
120 Vas. Sophias
Athens 115 26
Greece
www.intergenetics.eu

CONTACT DETAILS

mob: +30 693 2430633
E: genetics@otenet.gr, c.konialis@clingenics.co.uk

POSITIONS HELD - APPOINTMENTS

2002 - today	Head of the Department of Molecular Genetics and Genomics and Head of the Prenatal Biochemical Screening Unit, InterGenetics SA
1991 - 1999	Founder and Director of METROGEN SA, a private Biotechnology and Reference Laboratory, Athens, Greece
1986 - 1990	Research Associate in the Centre for Biological Research, National Hellenic Research Foundation (NHRF), Athens, Greece. Project Leader on: Molecular Genetics of Differentiation and Development of Human Erythropoietic Tissue
1984 - 1985	Post-doctoral research assistant in the Department of Biochemistry, University College London, working on a Biotechnology project involving cloning and expression of human recombinant pancreatic β-endorphin
1981 - 1983	Honorary Research Assistant - Demonstrator in the Department of Biochemistry, University College London

STUDIES - DEGREES

1979 - 1984	PhD in the laboratory of Prof. Peter H. W. Butterworth, Dept. of Biochemistry, University College London, London, UK Awarded Doctor of Philosophy (PhD) degree in 1984, University of London, for thesis on: "Molecular Cloning of Red Cell Carbonic Anhydrase I Coding Sequences"
1978 - 1979	Master of Science (MSc) course in Biochemistry Department of Biochemistry, University College London, London, UK Awarded MSc Degree in Biochemistry, University of London, July 1979
1973 - 1978	Undergraduate course in Chemistry (4 year course) Aristotelion University of Thessaloniki, Thessaloniki, Greece Received Degree in Chemistry in April 1978
1962 - 1972	Student at Athens College, Psychico, Athens, Greece High School Diploma in June 1972

BRIEF OVERVIEW OF WORK EXPERIENCE

In the last 15 years, I am Head of The Department of Molecular Genetics and Genomics and Head of The Prenatal Biochemical Screening Unit at InterGenetics SA, a private Medical Genetics center established in Greece in 1985. When I joined, the laboratory was executing in-house 2-3 very basic genetic tests. Over the years, I designed, developed and validated more than 200 new genetic tests, using multiple advanced techniques and platforms, thus being for many years the only laboratory in Greece and one of the few worldwide offering several of these tests. I have been responsible for: (a) managing and supervising the scientific personnel (4-5 laboratory scientists and 1 technician), (b) optimizing the workflow and (c) the final clinical reporting/sign-out of test results, covering a wide range of common and rare genetic disorders and syndromes. Genetic testing involved both postnatal and prenatal clinical investigations, for confirmation of diagnosis in affected individuals, carrier testing and prenatal diagnosis, as well as DNA Profiling for paternity and familial relationship testing.

In 2004 I was responsible for setting-up and implementing Preimplantation Genetic Diagnosis (PGD) for several single gene disorders, leading to *breakthrough pioneering clinical applications involving PGD coupled to HLA-matching in 2006*, with successful therapy of affected sibs (*see relevant scientific publications)*.

In mid-2006, I developed and introduced an expanded prenatal chromosomal testing panel (*EPP*) for the simultaneous targeted detection of 23 known recurrent microdeletion/microduplication syndromes, as well as subtelomeric copy number assessment for all chromosomes *(see relevant scientific publication)*. In late 2007, I established the chromosomal microarray (CMA-aCGH) unit and initiated postnatal clinical aCGH testing in patients with a syndromic phenotype, developmental delay, etc. A few years later, in early 2011, the laboratory implemented CMA as a standalone routine test in prenatal chromosomal diagnosis, being one of the first centers worldwide to introduce this approach as a routine test in a prenatal setting (*see relevant scientific publications)*.

Concurrently, aCGH was also applied in PGD for the detection of chromosomal aneuploidies (PGS) and, more importantly, for the detection of genomic imbalances in embryos resulting from parental translocations.

In summary, the techniques deployed over the years 2002-2010 in new assay development for various clinical applications included: singleplex and multiplex PCR, fragment and microsatellite analysis, QF-PCR, high-throughput automated DNA Sanger sequencing, CMA-aCGH, Multiple Ligation-dependent Probe Amplification (MLPA), High-Resolution Melting Curve Analysis (HRMA), multiplex SnaPshot and single-cell analysis through Whole Genome Amplification (WGA).

In late 2011, I established the in-house Next Generation Sequencing (NGS) genomics facility, based initially on the Illumina GAIIx platform and later on the Thermo Fisher Ion Proton System. NGS applications I developed and implemented included mainly clinical whole exome sequencing (WES) as well as the implementation of numerous multi-gene panels for a variety of disorders, such as neurogenetic disorders, epilepsy, cancers, etc.

Apart for clinical WES and multi-gene panels, novel genomic NGS applications I developed over the last 2 years include breakthrough applications of expanded targeted exome sequencing in fetuses with ultrasound abnormalities (the *Fetalis* test, *see relevant scientific publications*) and emergency neonatal-NICU whole exome sequencing (the *NeotaliStat* test, *reporting in 48 hrs*).

Indicatively, during the last 15 years, I have personally supervised, clinically evaluated and signed-out clinical genetic testing patient reports for:

- ~490 clinical cases involving Whole Exome Sequencing (single proband or WES-trio), for a variety of complex genetic disorders, such as neuromuscular disorders, neuro-developmental disorders, complex phenotypes in newborns, etc.
- ~280 multi-gene NGS panel testing in clinical cases involving hearing-loss, epilepsy, retinopathies, cardiogenetic disorders, breast cancer, various other types of cancer,
- ~650 other clinical cases, involving genetic testing for various genetic syndromes and monogenic disorders,
- ~15,000 prenatal and postnatal CMA (aCGH) and expanded chromosomal diagnosis cases,
- ~2,000 α- and β-thalassemia prenatal and postnatal cases,
- ~15,000 cystic fibrosis cases (diagnostic testing, carrier testing and prenatal testing),
- ~2,000 cases involving genetic testing for a variety of neurogenetic and neuro-developmental disorders,
- ~1,200 cases involving genetic testing for copy number variations in hematological malignancies
- ~90,000 prenatal chromosomal aneuploidy testing by QF-PCR,

In the last 5 years, I have also conducted and/or participated regularly in genetic counseling and clinical genetic evaluation of ~1,200 patients and families, for a wide range of cases/referrals, involving: syndromic and non-syndromic intellectual disability, various childhood and adult onset neurogenetic disorders, prenatal chromosomal diagnosis, abnormal prenatal ultrasound findings, repeated abortions and infertility, cancer syndromes, etc.

ClinGenics (UK) Ltd

Since 2012, and in close collaboration with Prof. Zach Agioutantis (currently Mining Engineering Foundation Professor at the University of Kentucky), I designed and implemented a comprehensive, multi-parametric, phenotype-driven, NGS variant prioritization and clinical interpretation bioinformatics pipeline (*Exome Management Application–EMA®*), together with *NGS-PanelBuilder®,* a clinical genomics decision support tool, both of which are being constantly refined and are now commercialized through ClinGenics (UK) Ltd. In brief, the ClinGenics *Exome Management Application-EMA®* pipeline software is a multi-parametric, phenotype-driven, powerful bioinformatics tool, coupled to expert manual curation, providing cutting-edge decision support for clinical interpretation of variants generated from clinical applications of Next

Generation Sequencing (NGS), involving primarily Whole Exome Sequencing (WES), but also single-gene and multi-gene NGS analysis.
The pipeline is intended exclusively for physicians and genetics professionals who need a tested and reliable tool to aid in their clinical investigation and final diagnosis of patients subjected to clinical exome sequencing studies. The final variant interpretation report provided by ClinGenics has the added important feature of incorporating expert manual curation, personalized interpretation and case-specific comments and suggestions for further actions, thus fulfilling its role as a true decision support tool (further details regarding the ClinGenics *Exome Management Application-EMA®* pipeline and *NGS-PanelBuilder®* are available upon request).

RESEARCH & DEVELOPMENT ACTIVITIES

1. Continuous involvement in the design and internally funded development of several novel clinical molecular genetics laboratory applications:
    - Design and implementation of a novel expanded targeted exome sequencing application in fetuses with ultrasound abnormalities (the *Fetalis* test - *see relevant scientific publications*)
    - Design and implementation of emergency neonatal-NICU whole exome sequencing (the *NeotaliStat* test – reporting in 48 hrs).
    - Design and subsequent implementation of a novel MLPA reagent/panel for routine detection of clinically relevant chromosomal deletions/duplications in haematological malignancies, eventually commercialized by MRC-Holland *(see relevant scientific publication).*
    - Validation and implementation of CMA as a standalone test in routine prenatal chromosomal diagnosis *(see relevant scientific publication)*,
    - Design and implementation of an expanded prenatal testing panel (*EPP*) for the targeted detection of known recurrent microdeletion/microduplication syndromes in fetuses *(see relevant scientific publication)*,
    - Design and implementation of a *routine* prenatal screening test for Fragile X and Spinal Muscular Atrophy (part of routine prenatal chromosomal diagnosis),
    - Design and implementation of a custom Greek mutation panel for cystic fibrosis testing, for the added detection of 11 common Greek CFTR gene mutations,
    - Design and implementation of protocols for Preimplantation Genetic Diagnosis (PGD) coupled to HLA-matching (*see relevant scientific publications)*

2. Project Initiator – Project Leader of the externally funded EEC (EU) *STRIDE* project: `DETECT' - Development and Applications of DNA-based Detection Systems in Identification and Diagnosis', January 1993-1995. Project budget: 332 million GRD (approx. 1,2 million USD).
    - The most notable achievement of the project was the development of novel DNA Profiling technologies (STR multiplexes) within EDNAP (see EDNAP meeting proceedings, Coimbra, Portugal, 1994, and EDNAP meeting proceedings, Athens, Greece, 1995) and the formal establishment of the Forensic DNA Laboratory of the Greek Police in 1994.

CONFERENCES AND PRESENTATIONS

Continuous participation, *involving almost exclusively oral platform presentations and invited talks,* in over 150 international and national conferences. Recent examples of international *oral platform presentations* include: ESHG Conference 2016, Barcelona, Spain; ASHG 2010 Annual Meeting, Washington, DC (full list available upon request).

TEACHING EXPERIENCE

Lecture on: 'Molecular Genetic Approaches for the Diagnosis of Leukemias', Postgraduate Seminars, Hematology Clinic, 'Laiko' Hospital, University of Athens Medical School, Athens, 2013.

Lecture on: 'Genetics of Hearing Loss and Deafness', Postgraduate Seminars, Otolaryngology Clinic, 'Laiko' Hospital, University of Athens Medical School, Athens, March 2009.

Lecturer in the Postgraduate Course: "Cellular and Genetic Etiology, Diagnosis and Treatment of Human Disease", Faculty of Medicine, University of Crete, 2005.

Instructor in the Postgraduate Course on: "Basic Techniques of Genetic Engineering" (EEC Course), Aristotelion University of Thessaloniki, 1988.

Lectures to undergraduate students (BSc) and post-graduate (MSc) Biochemistry students on the use and application of Genetic Engineering techniques, University College London, 1982-1984.

Lectures and supervision of Medical Students in Biochemistry laboratory projects, University College London, 1980-1984.

SUPERVISORY EXPERIENCE - OTHER SELECTED ACTIVITIES

Supervisor of 3 post-graduate PhD students at the Centre for Biological Research, NHRF, between 1985-1990.

Member of the panel for the evaluation of research projects submitted for funding to the Greek Science and Research Directorate within the framework of EPET II, 1995.

Organiser of the European DNA Profiling – EDNAP meeting, Athens, 1995.

Organiser of the 2-week Laboratory Course (funded by the Biotechnology program of the EEC) on: `Biomedical Applications of Genetic Engineering', Athens, October 1989.

Co-organizer of the Meeting-Seminars: "Genetic Engineering in Medicine", Patras, September 1988.

Coordinator-Greek Science and Research Directorate, 1986-1988, of research projects in Molecular Biology.

Member of the organizing committee of the Panhellenic Conference of the Greek Biologists Union on `Biology and Production', Sept. 1987.

Advisor-committee member on the design and implementation of the `Endorphin' Biotechnology project, University College London, 1983.

Since 1991, I have trained and supervised daily more than 40 Molecular Biologists-Molecular Geneticists (scientists and laboratory personnel at BS, MS and PhD level) in various aspects and techniques of molecular genetic testing.

PROFESSIONAL SOCIETIES – MEMBERSHIPS

Member of the British Society for Genetic Medicine (BSGM/ACGS)

Member of the American Society of Human Genetics (ASHG)

Member of the European Society of Human Genetics (ESHG)

Member of the European Society of Human Reproduction and Embryology (ESHRE)

Member of the Hellenic Association of Medical Geneticists

Member of the European DNA Profiling Group (EDNAP) 1992 - 1996

JOURNALS – EDITOR OR BOARD MEMBER

Member of Editorial Board – Journal of Pediatric Genetics (ISSN: 2146-4596)

PUBLICATIONS – PEER REVIEWED

1. **Konialis C**, Hagnefelt B, Karapanou S, Pangalos C
   Whole exome sequencing in a newborn with severe distal arthrogryposis reveals homozygosity for a paternal *ECEL1* gene mutation as a result of uniparental paternal isodisomy for chromosome 2
   (*manuscript in preparation*)
2. **Konialis C**, Lilakos K, Hagnefelt B, Karapanou S, Pangalos C
   A Microdeletion at Xp11.22 Detected by Whole Exome Sequencing Confirms *SHROOM4* Association with Stocco dos Santos Syndrome and XLID in a Large Kindred
   (*manuscript submitt*ed)
3. Gontika M, **Konialis C**, Pangalos C, Papavasiliou A
   Novel *SCN1A* and *GABRA1* gene mutations with diverse phenotypic features and the question on the existence of a broader spectrum of Dravet Syndrome
   Child Neurol Open. 2017 May 8;4:2329048X17706794
4. **Konialis C**, Asimakopoulos E, Hagnefelt B, Karapanou S, Sotiriadis A, Pangalos C.
   Prenatal diagnosis of X-linked Myopathy associated with a *VMA21* gene mutation afforded through a novel targeted exome sequencing strategy applied in fetuses with abnormal ultrasound findings.
   Clin Case Rep 2017;5:308–311.
5. Pangalos C, Hagnefelt H, Lilakos K, **Konialis C**
   First applications of a targeted exome sequencing approach in fetuses with ultrasound abnormalities reveals an important fraction of cases with associated gene defects.
   Peer J 2016 Apr 26;4:e1955.
6. **Konialis C,** Spengos K, Iliopoulos P, Karapanou S, Gialafos E, Hagnefelt B, Vemmos K, Zakopoulos N, Pangalos C
   The *APOE* E4 Allele Confers Increased Risk of Ischemic Stroke Among Greek Carriers
   Adv Clin Exp Med. 2016;25:471-8.
7. **Konialis C,** Pangalos C
   Dilemmas in prenatal chromosomal diagnosis revealed through a single center's 30 years' experience and 90,000 cases.
   Fetal Diagn Ther 2015;38(3):218-32.

8. Aravidis C, **Konialis CP,** Pangalos CG, Kosmaidou Z
A familial case of Muenke syndrome. Diverse expressivity of the *FGFR3* Pro252Arg mutation. Case report and review of the literature
J Matern Fetal Neonatal Med 2014;27(14):1502-6.

9. **Konialis C,** Savola S, Karapanou S, Markaki A, Karabela M, Polychronopoulou S, Ampatzidou M, Voulgarelis M, Viniou N, Variami E, Koumarianou A, Zoi K, Hagnefelt B, Schouten J, Pangalos C
Routine application of a novel MLPA based first line screening test uncovers clinically relevant copy number aberrations in haematological malignancies undetectable by conventional cytogenetics.
Hematology 2014;19(4):217-24.

10. **Konialis C,** Hagnefelt B, Sevastidou S, Pispili K, Pangalos C
A novel β^0-thalassemia frameshift mutation: codon 72(-T)[Hbb: c.216delT]
Hemoglobin 2012;36(6):586-8.

11. **Konialis C,** Hagnefelt B, Sevastidou S, Karapanou S, Pispili K, Markaki A, Pangalos C.
Uncovering recurrent microdeletion syndromes and subtelomeric deletions/duplications through non-selective application of a MLPA based extended prenatal panel in routine prenatal diagnosis.
Prenat Diagn 2011; 31:571-577.

12. Illmensee K, Levanduski M, **Konialis C,** Pangalos C, Vithoulkas A, Goudas V
Human embryo twinning with proof of monozygocity.
Middle East Fertility Society Journal 2011;16:215-219.

13. Goussetis E, **Konialis C,** Peristeri I, Kitra V, Dimopoulou M, Petropoulou T, Vessalas G, Papassavas A, Tzanoudaki M, Kokkali G, Petrakou E, Spiropoulos A, Pangalos C, Pantos K, Graphakos S
Successful hematopoietic stem cell transplantation in two children with X-linked chronic granulomatous disease from their unaffected HLA-identical siblings selected using pre-implantation genetic diagnosis combined with HLA-typing.
Biol Blood Marrow Transplant 2010;16:344-9.

14. Pangalos C, Hagnefelt B, Kokkali G, Pantos K, **Konialis C**
Birth of a healthy histocompatible sibling following preimplantation genetic diagnosis for chronic granulomatous disease at the blastocyst stage coupled to HLA typing
Fetal Diagn Ther 2008; 24(4): 334-9.

15. **Konialis C,** Hagnefelt B, Kokkali G, Pantos C, Pangalos C
Pregnancy following preimplantation genetic diagnosis of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL).
Prenat Diagn 2007 Nov;27(11):1079-83.

16. **Konialis CP,** Hagnefelt B, Kazamia C, Karapanou S, Pangalos C
CFTR DeltaF508 mutation detection from dried blood samples in the first trimester of pregnancy: a possible routine prenatal screening strategy for cystic fibrosis?
Fetal Diagn Ther 2007;22(1):41-4.

17. Milunsky A, **Konialis C,** Shim SH, Maher TA, Spengos K, Ito M, Pangalos C
The prenatal diagnosis of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) by mutation analysis.
Prenat Diagn 2005;25(11):1057-8.

18. **Konialis CP**
Current molecular genetic approaches to the laboratory investigation of Y-chromosome microdeletions in infertile men
Anir 2001;4:175-179.

19. Andersen J, Martin P, Carracedo A, Dobosz M, Eriksen B, Johnsson V, Kimpton C, Kloosterman A, **Konialis C,** Kratzer A, Phillips P, Mevag B, Pfitzinger H, Rand S, Rosen B, Schmitter H, Schneider P, Vide M
Report on the third EDNAP collaborative STR exercise. European DNA Profiling Group.
Forensic Sci Int 1996;78(2):83-93.

20. Levedakou EN, **Konialis CP,** Sekeris CE
Vitellogenin mRNA from *Dacus oleae*: Characterization, cDNA cloning and dependence on sex and developmental stage.
Arch Insect Biochem Physiol 1988; 9(2):119 – 134.

21. Edwards YH, Barlow JH, **Konialis CP**, Povey S, Butterworth PHW
Assignment of the gene determining human carbonic anhydrase, CAI, to chromosome 8.
Ann Hum Genet 1986;50(2):123-9.

22. Butterworth PHW, **Konialis CP**, Barlow JH, Povey S. and Edwards Y
Cytogenet Cell Genet 1985;40:567-569.

23. Konialis CP, Barlow JH, Butterworth PHW
Cloned cDNA for rabbit erythrocyte carbonic anhydrase I: A novel erythrocyte-specific probe to study development in erythroid tissues.
Proc Natl Acad Sci USA 1985 Feb;82(3):663-7.

Approximately 60% first or last author publications

Ph.D Thesis: Konialis C. Molecular Cloning of a cDNA Coding for the Red Cell Marker Carbonic Anhydrase I, University College London – University of London; 1984

COMPUTER SKILLS

Expert level. IT Administrator at current positions

Operating systems:
Windows NT, Windows XP, Windows 7, Windows 10, Windows 2000-2012 server, Mac OS

Software:
Microsoft Office, SQL Server, SoftGenetics GeneMarker, SoftGenetics Mutation Surveyor, SoftGenetics NextGENe, and many other bioinformatics applications in Genetics and Genomics

Hardware:
Server setup and deployment (Windows-based servers), network setup and network security (routers, TCP/IP, switches/hubs, raid/mirror, backup, etc.)

LANGUAGE SKILLS

English: native speaker/proficient user (fluent, both reading and writing)

French: basic communication skills/working knowledge

Italian: basic user

PERSONAL DATA

Home Address:

- 232 Castle Rd, Bedford, MK40 3UA, United Kingdom

Married to Swedish-born Birgitta Hagnefelt, Molecular Geneticist.
Two daughters, Elianna Konialis, age 37, and Christina Konialis, age 35

Personal interests:

- Sports:

  Sailing (regularly since childhood, inshore and offshore racing, 2nd place 1995 Greek Offshore Racing IOR-IMS championships and many other offshore and inshore regatta placings)

  Equestrian (1994-2002, show-jumping at advanced level, winner or in top 6 of ~30 national events and shows up to Level 8 - fences up to 4'9" in height)

  Squash (regularly)

  S*occer* (regularly)

- Reading
