Per una “G” in più

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Il Presidente Antonio Antoccia mi ha invitato a commentare ed a ricordare le radici storiche del cambiamento di denominazione della Società da SIMA a SIMAG, a distanza di 5 lustri dalla sua istituzione. Infatti la Società Italiana di Mutagenesi Ambientale (SIMA) venne fondata nel luglio 1991, diventando la Sezione italiana della European Environmental Mutagenesis Society (EEMS, fondata nel 1969), a sua volta afferente all’International Association of Environmental Mutagen Societies (IAEMS, fondata nel 1973), che comprende attualmente 13 sezioni regionali. Da 15 anni la SIMA è anche affiliata, con altre 13 Società nazionali, alla Federazione Italiana di Scienze della Vita (FISV).

Il primo Presidente SIMA fu Nicola Loprieno, e il primo Meeting annuale venne organizzato a Pisa da Giorgio Bronzetti nell’ottobre 1992. Il Meeting ebbe notevole successo, condensando in due giorni 58 presentazioni a nome di 190 ricercatori, per la maggior parte italiani ma con importanti contributi di scienziati provenienti da altri paesi, come Bulgaria, Croazia, Finlandia, Francia, Germania, Olanda, UK e USA [De Flora S. Meeting Report. First Annual Meeting of the Italian Section of the European Environmental Mutagen Society (SIMA). *Mutat. Res. Rev. Genetic Toxicol.* 291, 217-222, 1993].

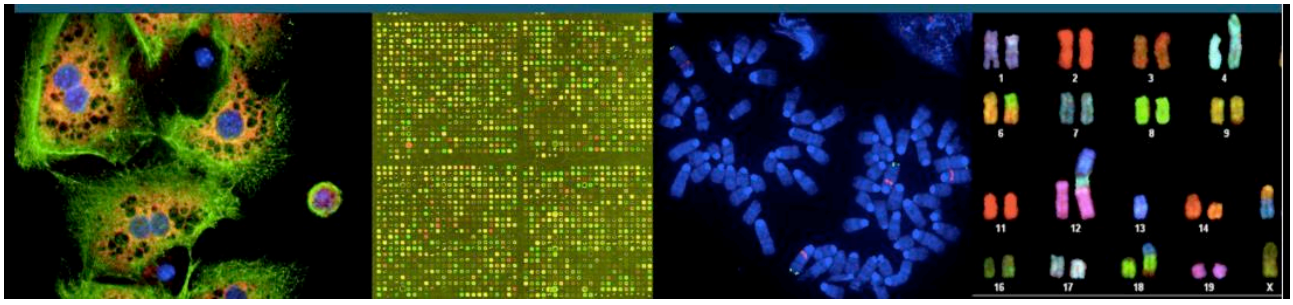
Dieci anni orsono, quando organizzammo la 10ª International Conference on Environmental Mutagens (X ICEM, Firenze, 20-25 agosto 2009), cominciò a farsi strada l’idea che le denominazioni delle Società di Mutagenesi Ambientale non erano più soddisfacenti e non riflettevano appieno l’attività scientifica di molti soci. A quell’epoca David D. DeMarini era Presidente IAEMS per il periodo 2005-2009 (con Angelo Carere Vice-Presidente) e gli stava per subentrare Stefano Bonassi, Presidente per il periodo 2009-2013. Mi ricordo che David era venuto a trovarci a Genova per l’organizzazione dell’ICEM a Firenze e lo invitammo a visitare Portofino. Fu lì, passeggiando sul molo del porticciolo, che discutemmo la questione della denominazione delle Società e mi venne l’idea di aggiungere in qualche modo la parola-chiave “Genomica”. Nel corso della sua Presidenza, Stefano chiese a David ed a me di interessarci del cambiamento di denominazione.

Con David pubblicammo un articolo sull’argomento [DeMarini D.M., De Flora S. What’s in a name? The argument for changing the name of IAEMS and its affiliated Societies. *Mutat. Res. Rev. Genetic Toxicol.* 705, 201-204, 2010]. Come discutemmo in dettaglio in quell’articolo, c’erano vari motivi

di insoddisfazione per le attuali denominazioni. Anzitutto il termine di "mutagenesi ambientale" era poco appealing e per di più poco comprensibile ai colleghi di altre discipline. Inoltre vi era stato un declino o una mancanza di crescita dei soci di alcune delle società che avevano fondato l'IAEMS, come la società europea (EEMS), quella nord-americana (EMS) e quella giapponese (JEMS). C'era anche stata una diminuzione delle pubblicazioni riguardanti l'applicazione di test classici di mutagenesi. Come documentato da Larry Claxton *et al.* [The Salmonella mutagenicity assay: The stethoscope of genetic toxicology for the 21st century. *Environ. Hlth Perspect.*, 118, 1515-1522, 2010], dall'analisi di 35.000 articoli pubblicati dal 1970 risultava che a metà degli anni '80 del 1900 venivano pubblicati 500 articoli all'anno sul test della Salmonella, che si erano ridotti a 200 nel decennio 2001-2010. Durante gli ultimi 25 anni, solo 20-30 articoli all'anno riguardarono test di mutagenicità in cellule di mammifero. Gli articoli sul micronucleo raggiunsero un massimo di 100 all'anno all'inizio dei primi anni '90 del 1900, per poi rimanere sugli stessi livelli, e gli articoli sul comet raggiunsero un plateau di 700 all'anno.

Dagli anni '90 del 1900 la scienza della tossicologia genetica ridusse la sua area di interesse, anche a livello di finanziamento di ricerche. Per contro vi fu un'enorme crescita della genomica e delle sue applicazioni alla medicina, scienze ambientali e sanità pubblica. Questo vale soprattutto se, come suggerito dall'US EPA (epa.gov/osa/spc/dfs/genomics.pdf), il termine genomica in senso lato acquisisce un significato più ampio, abbracciando non solo effetti al livello del DNA (genoma in senso stretto), mRNA (transcriptoma) e proteine (proteoma) ma anche effetti epigenetici al livello di microRNA (mirnoma), modificazione degli istoni, ecc. In effetti, già dagli anni 2000 le Società di Mutagenesi Ambientale avevano incluso argomenti di genomica nei programmi dei loro meeting.

Dopo varie discussioni a livello societario, alcune Società aggiunsero una "G" (Genomics) alla loro denominazione e relativo acronimo. Così, nell'autunno 2013, l'IAEMS diventò IAEMGS (International Association of Environmental Mutagenesis and Genomics Societies). Da notare che, oltre all'aggiunta della "G" di "Genomics", "Mutagen" venne trasformato in "Mutagenesis", termine che appare più appropriato. Ancora prima, alla fine del 2012, la Società nord-americana (EMS) cambiò la sua denominazione in EMGS (Environmental Mutagenesis and Genomics Society) [Wilson T.E. *et al*.,Building on the past, shaping the future: the Environmental Mutagenesis and Genomics



Society. *Environ. Mol. Mutagenesis*, 54, 153-157, 2013]. L'immagine riportata dal sito EMGS (https://www.2mgs-us.org/p/cm/ld/fid=72), riflette chiaramente non solo il cambiamento di denominazione ma anche l'ampliamento dei contenuti e delle metodologie utilizzate, con la missione di "promuovere la conoscenza critica e la ricerca scientifica sulle cause e conseguenze del danno al genoma e all'epigenoma…". Come scritto dall'allora Presidente IAEMS Stefano Bonassi in una lettera circolare ai Presidenti delle sezioni regionali, "a special recognition should be given to David and Silvio who transformed our feelings that the old name should be reconsidered in a circumstantiated position paper providing evidence about the inevitable change". Anche la Società brasiliana divenne Brazilian Association of Mutagenesis and Environmental Genomics. Nel 2016 venne approvato e finalizzato il cambiamento di nome della Società europea da EEMS a EEMGS (European Environmental Mutagenesis and Genomics Society), con 112 voti favorevoli su 115. Questa decisione maturò dopo diversi anni di discussione. Ho copia di una lettera autorevole di Radim Sram, datata luglio 2011, all'allora Presidente EEMS Jeffrey Schwartz in cui Radim scriveva: "Yes, I support your activity to change the name of the Society. I am probably one of the few founding members (already from 1969!), therefore I was not originally too much in favor of that change. But to be realistic, as time is changing, probably the new name Environmental Genomic Society will be more corresponding to our tasks in the future. Simultaneously I believe it should increase our membership as well as improve our public image". Giustamente, l'espressione "environmental genomic", che può apparire un po' contraddittoria, venne poi sostituita da "environmental mutagenesis and genomics".

In precedenza, durante il mio periodo di Presidenza della SIMA (2008-2010), avevo proposto ai Soci, sia durante l'assemblea che per ballottaggio telematico, di cambiare la denominazione della nostra Società. In entrambe le occasioni quasi tutti i Soci si dichiararono favorevoli ad un cambiamento di denominazione e la maggioranza votò anche a favore della proposta di aggiungere una "G" al nome. Tuttavia non vi era unanimità sul secondo punto, per cui preferii soprassedere e non prendere una decisione che non fosse condivisa e gradita da tutti. Ora il Presidente Antonio Antoccia mi ha comunicato che, con una prima delibera del 21 settembre 2016 e successiva delibera del 25 settembre 2017, è stata ufficialmente approvata la "mutazione" da SIMA a SIMAG. La gestazione è stata un po' lunga e travagliata ma si è conclusa felicemente e i relativi documenti sono stati depositati presso il notaio il 26 febbraio 2018 (giorno della nevicata a Roma!). Mi auguro che, con la nuova denominazione, possano entrare a far parte della SIMAG altri Soci che apportino nuovi contributi scientifici da affiancare al patrimonio tradizionale della Società.

Mutation Research, 291 (1993) 217–222

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Meeting Report

First Annual Meeting of the Italian Section of the European Environmental Mutagen Society (SIMA)

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The First Annual Meeting of the Italian Section of EEMS (SIMA, Società Italiana di Mutagenesi Ambientale) was held in Pisa on 7–8 October 1992 at the 'Palazzo dei Congressi'. SIMA was founded on 5 October 1991 in Alghero, where Nicola Loprieno had been elected President, Angelo Carere Vice-President, Angelo Abbondandolo, Roberto Barale, Giorgio Cantelli-Forti, Luigi De Carli, Silvio De Flora and Angelo G. Levis members of the Directive Council, and Francesca Pacchierotti Secretary-Treasurer. One of the first tasks of the Directive Committee, which had been scheduled to remain in charge until the First Annual Meeting, was to make a review of the applications for membership, to be updated at each annual meeting. Based on rather selective criteria of the curricula submitted, especially concerning the scientific production in internationally reputable journals, 123 members were accepted as members of SIMA at the end of the starting year of activity.

In his presidential address to the General Assembly in Pisa, Nicola Loprieno (University of Pisa) stressed that the foundation of SIMA was a formal act, aimed at officializing in a national section the contribution given by Italian investigators in the framework of EEMS and IAEMS during the past two decades.

The scientific program of the meeting was introduced by Angelo Abbondandolo (IST and University of Genoa) and by Giorgio Bronzetti (CNR, Pisa), who successfully acted as the chairman of the local Organizing Committee and took care of the preparation of the proceedings including the abstracts of all oral and poster presentations.

Mechanisms of genic, chromosomic and genomic mutations

Invited lectures

The first day of the meeting was entirely devoted to a symposium on the general theme of mechanisms of mutation. The morning session, which was chaired by Stefania Bonatti (CNR, Pisa) and Angelo Abbondandolo, included five invited lectures.

David M. DeMarini (U.S. Environmental Protection Agency, Research Triangle Park, NC, USA), a scientist of Italian origin, gave a quite interesting presentation dealing with the mutation spectra and molecular mechanisms of mutations induced by urban air and other complex

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Commentary

What's in a name? The argument for changing the name of IAEMS and its affiliated societies

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ABSTRACT

We identify trends over the past decades in membership in societies affiliated with the International Association of Environmental Mutagen Societies (IAEMS), and we also highlight findings in a recent review by Claxton et al. [Environ Health Perspect, in press] regarding the numbers of papers published per year using genetic toxicology assays. These analyses reveal a decline or at best a static level of membership in IAEMS-affiliated societies, as well as a decline in the number of papers published per year using genetic toxicology assays—with the exception of those using comet assays, which already have begun to plateau. In contrast, toxicogenomics and computational toxicology are becoming increasingly prominent relative to environmental mutagenesis research in most research institutes, reflecting the ascendancy of these areas of environmental toxicology. We conclude that changing the name of IAEMS and its affiliated societies to reflect these changes might enhance membership and publication by welcoming a broader range of scientists into these societies. Although various names are possible, we think that changing the name of these societies to "Environmental Genomics Society" may help to make our societies more attractive to a broader range of scientists, resulting in an increase in membership and an acceleration of the incorporation of genomic methods into environmental research.

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1. Introduction

The IAEMS and some of its initial member societies, such as the EMS, EEMS, and JEMS, have reached or are approaching 40 years of age [1], and this provides an opportunity to reflect on both the past successes and future opportunities of IAEMS. In particular, we should use this occasion to consider the developments in the field of environmental mutagenesis and to assess the membership of the societies, the scientific trends in our field, and possible changes that might revitalize our societies and welcome new members from new areas of science.

While one of us (DeMarini) was President of the IAEMS (2005–2009), he initiated a conversation among the leadership of the various IAEMS-affiliated societies to explore the idea of changing the name of IAEMS and its societies. The reasons for this are outlined below. However, this effort was informal and did not proceed to the level of a formal proposal to the societies. Consequently, the new President of the IAEMS, Stefano Bonassi, appointed both of us to formalize the arguments for changing the name and to present our thoughts to the IAEMS Executive Board and Council for consideration and discussion—with a final version of the argument to be presented to the leadership and members of the affiliated societies for further discussion.

To address this issue, we review in this Commentary the current diversity of names of the IAEMS-affiliated societies, as well as the lack of clarity and visibility of these names to scientists (and certainly to non-scientists) outside of our field. We also present a brief historical review of (a) the membership of the IAEMS-affiliated societies, (b) the decline in environmental mutagenesis research in some public institutions, and (c) the numbers of publications in the specific area of genetic toxicology over the past 40 years. Based on these various considerations, we then suggest several possible new names, with the aim of placing any proposed new name within the context of contemporary science. Finally, we review some of the obstacles to changing the name, as well as summarize our position on this matter.

2. The problem of recognition of our current name

The IAEMS-affiliated societies have a variety of names already and exhibit some diversity in this regard. Some of the examples include the Latin American Association of Environmental Mutagenesis, Carcinogenesis, and Teratogenesis (ALAMCTA) and the Mutagenesis and Experimental Pathology Society of Australasia (MEPSA). In addition, most of us have had the experience of telling a scientist (and certainly non-scientists) that we do environmental

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Environmental and Molecular Mutagenesis 54:153–157 (2013)

Commentary

Building on the Past, Shaping the Future: The Environmental Mutagenesis and Genomics Society

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In late 2012, the members of the Environmental Mutagen Society voted to change its name to the Environmental Mutagenesis and Genomics Society. Here, we describe the thought process that led to adoption of the new name, which both respects the rich history of a Society founded in 1969 and reflects the many advances in our understanding of the nature and breadth of gene-environment interactions during the intervening 43 years. Environ. Mol. Mutagen. 54:153–157, 2013. © 2013 Wiley Periodicals, Inc.

Key words: genetics; epigenetics; toxicology; DNA repair; mutation research; mutagen

HISTORICAL FOUNDATION

A detailed history of the Environmental Mutagen Society (EMS) has been recounted previously [Wassom, 1989; Wassom et al., 2010]. The EMS was founded in 1969 by a group of distinguished scientists that included Alexander Hollaender, Joshua Lederberg, James Crow, James Neel, William Russell, Heinrich Malling, Frederick J. de Serres, and Matthew Meselson (www.emgs-us.org). The goals and interests of the Society were and are to promote research and training of scientists in the fields of environmental mutagenesis and genetic toxicology to promote human health by minimizing exposure risks.

Additional Supporting Information may be found in the online version of this article.

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The *Salmonella* Mutagenicity Assay: The Stethoscope of Genetic Toxicology for the 21st Century

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Objectives: According to the 2007 National Research Council report *Toxicology for the Twenty-First Century*, modern methods (e.g., "omics," *in vitro* assays, high-throughput testing, computational methods) will lead to the emergence of a new approach to toxicology. The *Salmonella* mammalian microsome mutagenicity assay has been central to the field of genetic toxicology since the 1970s. Here we document the paradigm shifts engendered by the assay, the validation and applications of the assay, and how the assay is a model for future *in vitro* toxicology assays.

Data sources: We searched PubMed, Scopus, and Web of Knowledge using key words relevant to the *Salmonella* assay and additional genotoxicity assays.

Data extraction: We merged the citations, removing duplicates, and categorized the papers by year and topic.

Data synthesis: The *Salmonella* assay led to two paradigm shifts: that some carcinogens were mutagens and that some environmental samples (e.g., air, water, soil, food, combustion emissions) were mutagenic. Although there are > 10,000 publications on the *Salmonella* assay, covering tens of thousands of agents, data on even more agents probably exist in unpublished form, largely as proprietary studies by industry. The *Salmonella* assay is a model for the development of 21st century *in vitro* toxicology assays in terms of the establishment of standard procedures, ability to test various agents, transferability across laboratories, validation and testing, and structure–activity analysis.

Conclusions: Similar to a stethoscope as a first-line, inexpensive tool in medicine, the *Salmonella* assay can serve a similar, indispensable role in the foreseeable future of 21st century toxicology.

Key words: Ames assay, carcinogenicity, 21st century toxicology, genetic toxicology, high-throughput assays, *Salmonella* assay, *Salmonella* mutagenicity assay. *Environ Health Perspect* 118:1515–1522 (2010). doi:10.1289/ehp.1002336 [Online 2 August 2010]

Every day throughout the world, physicians, nurses, and an array of other health professionals use a stethoscope, which was invented by René Laennec in 1816 (Weinberg 1993). It is a relatively simple instrument whose sounds can indicate a myriad of disease states that can then be confirmed by more sophisticated assessments. It is hard to visualize a physician or imagine medicine without the stethoscope. Similarly, the *Salmonella* mutagenicity assay, which was developed initially as a spot test (Ames 1971), then as a plate-incorporation test (Ames et al. 1972) using strains of *Salmonella* bacteria derived from studies by B.N. Ames and P.E. Hartman (Hartman et al. 1986) and rodent liver microsomal activation coupled initially to the assay by H.V. Malling (Malling 1971), is a deceptively simple tool that can be used to detect the mutagenicity of environmental chemicals, environmental mixtures, body fluids, foods, drugs, and physical agents. More complex tests can be applied to confirm and characterize further the mutagenic activity of the agent. Although neither the stethoscope nor the *Salmonella* assay provides a definitive diagnosis/detection of a disease or a mutagen, respectively, both are indispensible first-line tools in their fields.

There is much unrest in the field of toxicology today because of a variety of scientific developments, including advances in genomic science (Parsons et al. 2008; Wood et al. 2007), improved knowledge of the molecular and mechanistic basis for biological responses to toxicant exposure (Guyton et al. 2009), legislation mandating reduced numbers of animals for toxicology testing (Pfuhler et al. 2009), and governmental direction to incorporate all of the above into a new paradigm for toxicology for the 21st century (National Research Council 2007).

A strict parallel cannot be drawn between a targeted testing assay such as the *Salmonella* assay, which is used for hazard identification, and a high-throughput screening (HTS) assay such as either the ToxCast program [U.S. Environmental Protection Agency (EPA)] or the combined U.S. EPA/National Institutes of Health (NIH)/National Institute of Environmental Health Sciences (NIEHS)/National Toxicology Program (NTP) Tox21 program (Kavlock et al. 2009), which can identify specific signaling or biochemical pathways relevant to potential disease development and thus have the possibility of going beyond hazard identification. An assay like the *Salmonella* assay is a stand-alone screen that requires high accuracy and reproducibility and is correlated with health end points, permitting its use for regulatory purposes. In contrast, HTS assays use emerging technologies and target probes, knowledge of biochemical and disease pathways in rodents and humans, genomics, and other technologies to generate a profile or pattern of effects across a range of chemical classes and biological end points that do not depend greatly on any particular chemical or assay result. As with the *Salmonella* assay, HTS assays are viewed as a first-line screening tool, with results of interest being followed up by more extensive confirmatory assays.

In the process of developing and adopting new methods, it is important to build on and learn from past paradigm shifts, several of which occurred in the field of genetic toxicology with the introduction of the *Salmonella* assay. Consequently, the history of the *Salmonella* assay highlights some of the necessary steps and considerations needed for the development of almost any type of toxicology assay, including some aspects of HTS assays. Our purpose with this review is to *a*) describe the paradigm shifts precipitated by the *Salmonella* assay, including the demonstration of a connection between mutagenicity and carcinogenicity and the ubiquitous nature of mutagens in our environment; *b*) document the historic and current applications of the *Salmonella* assay; and *c*) illustrate the lessons learned from the development, validation, testing, assessment, and uses of this *in vitro* assay that may be applicable to the development of *in vitro* toxicology assays for the 21st century.

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