

## On the future contents of a small journal of histochemistry

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### Abstract

In the last three years, more than 70,000 scientific articles have been published in peer reviewed journals on the application of histochemistry in the biomedical field: most of them did not appear in strictly histochemical journals, but in others dealing with cell and molecular biology, medicine or biotechnology. This proves that histochemistry is still an active and innovative discipline with relevance in basic and applied biological research, but also demonstrates that especially the small histochemical journals should likely reconsider their scopes and strategies to preserve their authorship. A review of the last three years volumes of the *European Journal of Histochemistry*, taken as an example of a long-time established small journal, confirmed that the published articles were widely heterogeneous in their topics and experimental models, as in this journal's tradition. This strongly suggests that a journal of histochemistry should keep its role as a forum open to an audience as broad as possible, publishing papers on cell and tissue biology in a wide variety of models. This will improve knowledge of the basic mechanisms of development and differentiation, while helping to increase the number of potential authors since scientists who generally do not use histochemistry in their research will find hints for the applications of histochemical techniques to novel still unexplored subjects.

### Introduction

Especially in the last few years, the number of open-access journals in the biomedical field has dramatically increased,<sup>1</sup> and this tendency is still continuing. As a consequence, when cell and tissue biology is considered, new competitors are adding every day to the traditional journals on histochemistry. Most of the new open-access journals are not yet indexed, and their quality and peer-reviewing strictness are questionable; this surely makes the journals with established reputation still preferable for scientists, although special offers for manuscript publication are often proposed by the new jour-

nals which may be appealing in the present situation of generalized grant shortening.

Under this scenario, especially the small journals should probably reconsider their scope and strategies, in the attempt to preserve their readership and the possibility to receive a sufficient number of good manuscripts to be selected for publication. Survival of a journal depends on the capability of saving and extending its authorship, and to this aim the present trends in the application of histochemistry should be considered while taking into account the authors' interests as they result from the articles published in recent years.

### Histochemistry in the biomedical field in recent years

The title of the last 54<sup>th</sup> Symposium of the Society for Histochemistry held in Vienna, last September 5-8, 2012 (<http://www.histochemistry54.eu/>) was *Imaging development: tracking cells in order and disorder*, the main topic being stem cell commitment and differentiation during normal development of invertebrate and vertebrate *taxa* as well as aberrant differentiation and de-differentiation under pathological conditions. The goal of understanding normality through the integrated analyses of structural, molecular and dynamic features of tissues and cells was one of the *take-home messages* of this Conference, thus underlying the unique opportunities provided by the histochemical approach in the attempt to describe basic mechanisms of cell proliferation, differentiation and death during normal development or under physiological conditions, and to discriminate altered pathological traits: this may be achieved only through the application of refined histochemical methods and novel microscopy techniques to detect specific molecular components at high resolution, as several presentations in the Symposium have actually demonstrated.

Biological processes in tissues, cells and subcellular compartments can only take place in a spatially organized environment, and an accurate description of these phenomena may be obtained by correlating the structural features to the composition and location of molecular markers: to this purpose, the microscopical and histochemical approach is definitely irreplaceable especially when the biological samples under investigation are characterized by an intrinsically complex and heterogeneous organization at the tissue, cell or organelle levels. This is one of the reasons why Histochemistry has been increasingly used in the biological research becoming a common tool for scientists in a wide variety of disci-

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plines investigating biology from the molecular to the organism level: this is apparent if we consider that, in the last three years, more than 70,000 scientific articles have been published in peer reviewed journals on the application of histochemistry in the biomedical field, with more than 22,000 articles per year during the 2000-2012 period (source: <http://www.ncbi.nlm.nih.gov/pubmed/>).

Thus histochemistry proves to be a still active, productive and innovative discipline with broad application not only in basic biological research, but also in the diagnostics of human and animal diseases where histochemistry continues to be a reliable and sometimes unique tool integrating and validating the results of the widely used molecular bioassays.<sup>2</sup> Consistently, the journals reporting articles where histochemistry is exploited have progressively increased in number, over the last decades; however, the journals strictly devoted to histochemistry are the most appropriate and up-to-date source of information both for the novel technical achievements and the application on new biological models. In addition, a survey, over a given timespan, of the articles' contents may suggest the recent tendencies in histochemists' interests and help to envisage their future evolution: a journal which traditionally covers a broad range of research subjects may represent a simplified model for such a review.

### A survey of the recent contents of a long-time established histochemical journal

The *European Journal of Histochemistry* is an example of a long-time established journal which has been uninterruptedly published

since 1954: as the official organ of the Italian Society of Histochemistry, since its very first issue it publishes reports on investigations by scientists from all over the world, on a wide variety of biological and biomedical subjects. In the present survey, the 130 articles issued in the last three years have been considered, and their contents compared with those published in the first ten years of publication of the journal (1954-1963) and in the ten-year period 2001-2009. The articles published in 2010-2012 have been classified into the few main topics, as selected in a previously published comment,<sup>3</sup> namely *Animal biology & veterinary medicine*, *Human biology & histopathology*, *Methods & techniques*, *Stem cells & development*, *Neurobiology & endocrinology*, *Cell nucleus*, *Muscle tissue*, *Connective tissue*, *Cell proliferation & death*, *Plant cell biology* (Figure 1 reports the distribution of the papers in the different subjects).

In the last three years, more than 45% of the articles fall into the first two categories, confirming the trend of histochemical research especially in recent years:<sup>2,3</sup> actually, more than 90% of the scientific articles applying histochemistry or immunohistochemistry that have been published in peer reviewed journals, since January 2010 to date, concerned pathological conditions in humans or other vertebrates (source: <http://www.ncbi.nlm.nih.gov/pubmed/>).

In the last-three-years sample from the *European Journal of Histochemistry*, several articles concerned the search for one or more diagnostic and prognostic indicators specifically marking a given disease,<sup>4-15</sup> but other were focussed on experiments aimed at identifying the molecular bases of the pathogenetic process,<sup>16-20</sup> or at assessing the metastatic potential of tumour cell populations,<sup>21,22</sup> or at describing the effects of therapeutic interventions.<sup>23-27</sup> Most of these studies were performed by light (essentially conventional or confocal fluorescence) microscopy, but electron microscopy and ultrastructural immunohistochemistry has also been used for investigating functional changes in cells from different tissues or under different experimental conditions.<sup>28-37</sup> To localize specific nuclear components, multiple immunohistochemical techniques and quantitative analyses of the immunogold labelling have been utilized,<sup>38</sup> and this approach proved to be especially appropriate to detect the alteration in transcription and splicing which characterizes specific diseases.<sup>24,31,39</sup>

Actually, the changes in the organization and molecular composition of nuclear domains are well established markers of changed cellular metabolism or cell dysfunctions related to pathological phenotypes.<sup>40,41</sup> The application of techniques of nuclear histochemistry in paral-

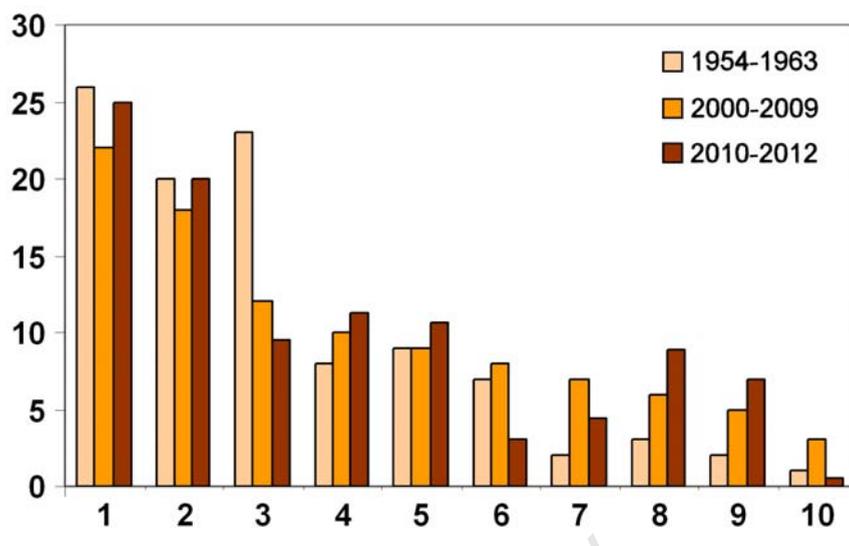


Figure 1. Percentage of the articles on different subjects published in the *European Journal of Histochemistry* during the ten-years periods, 1954-1963 and 2001-2009, and in the last three years, 2010-2012. The article subjects reported in the abscissa are as follows: 1. Animal biology & veterinary medicine; 2. Human biology & histopathology; 3. Methods & techniques; 4. Development & stem cells; 5. Neurobiology & neuroendocrinology; 6. Cell nucleus; 7. Muscle tissue; 8. Connective tissue, bone & cartilage; 9. Cell proliferation & death; 10. Plant cell biology.

lel with biomolecular methods allowed to demonstrate basic mechanisms of some muscle diseases characterized by altered organization of nuclear structures,<sup>29,39</sup> and revealed intriguing similarities in the origin of muscle atrophy in sarcopenia and myotonic dystrophy: this was demonstrated by studies on skeletal muscle *ex vivo* as well as on cultured myoblasts and myotubes *in vitro*.<sup>31,37,42</sup> Interesting results have also been reported on the expression of different cytoplasmic or nuclear proteins of mammalian myocytes and heart muscle cells during differentiation or aging,<sup>43</sup> or under physiologically or experimentally induced conditions of inactivity, physical exercise or oxidative stress.<sup>33,44-46</sup>

Several articles have also been published on normal human or animal cytology and histology: though being sometimes descriptive in nature (this is especially true for non-human animal *taxa*),<sup>47-66</sup> their scope was often to identify specific features within heterogeneous human tissues or cell populations, in view of possible applications in therapy or regenerative medicine.<sup>30,32</sup> Electron microscopy and ultrastructural cytochemistry have largely been used for such studies, confirming the importance of associating morphostructural evidence and molecular composition at high-resolution.

Most of the investigations performed on non-human vertebrates were aimed at monitoring the effects of different kind of stress (such as intoxication, infection, environmental pollution, or ischemia/reperfusion) through

the histochemical detection of altered organization or chemical in different organs and tissues.<sup>27,28,67-75</sup>

Developmental (including reproductive) biology received increasing interest, in the last three years, with papers devoted to the reproductive system,<sup>76,77</sup> with special attention to the expression of hormones or hormone receptors,<sup>56,78</sup> articles have been published on oocyte differentiation, elimination *in vivo*, and cryopreservation,<sup>34,35,79</sup> or the expression of growth factor or proliferation/differentiation markers during development of humans<sup>80,81</sup> and non-human vertebrates.<sup>49,82-86</sup> It is worth noting that several articles were especially focussed on neurobiology and endocrinology during embryogenesis,<sup>87-89</sup> post-natal development<sup>90-92</sup> or aging.<sup>93</sup> Most of the papers on stem cell biology concerned precursors of mesenchymal origin from the adipose tissue,<sup>30,32</sup> cartilage<sup>86,94</sup> or bone;<sup>95,96</sup> the attempts to elucidate some of the mechanisms responsible for their commitment and differentiation *in vitro* were often aimed at designing suitable strategies for their application in tissue engineering or plastic and reconstructive medicine.<sup>30,32,94,96</sup> In this perspective, it becomes primarily important to discriminate cells in the different phases of proliferation, differentiation, aging and death, through specific molecular markers: multiple immunocytochemical techniques were widely applied to this aim.<sup>24,31,38,43,45,97-99</sup> A manuscript only was devoted to plant cell development,<sup>100</sup> and this confirms that histochemistry is still relatively poorly used by plant biologists in

their research: actually, in the last three years, only 30 papers have been published, in which histochemical techniques have been used in investigations on plant cell biology (source: www.scopus.com). In recent years, connective tissues and, in particular, bone and cartilage have become increasingly popular subjects for the authors of the *European Journal of Histochemistry*.<sup>94,101-107</sup> Histochemistry proved to be especially suitable for investigating structure and function of the articular disc under different experimental and pathological conditions, with special reference to the temporomandibular joint.<sup>86,97,102,104,105,108,109</sup> In addition, two supplements have been published, collecting the abstracts of the XXXI and XXXII National Meeting of the Italian Society for the Study of Connective Tissues (SISC).<sup>110,111</sup>

Notes on methods and techniques have been fewer than in the previously considered periods: though being more addressed to the application of established techniques in cell and tissue biology, the authors of the *European Journal of Histochemistry* did however pay attention also to setting up innovative tools<sup>112-117</sup> or implementing conventional methods.<sup>118-124</sup> Cytogenetic techniques have been used to identify repetitive DNA sequences in the genome of humans and other vertebrates.<sup>121,125,126</sup>

## Concluding remarks

In a review article<sup>127</sup> summarizing the papers published in *Histochemistry and Cell Biology* during 2011, Stefan Huebner and Athina Efthymiadis underlined that the studies published in that journal *represent once more a manifest of established and newly sophisticated techniques being exploited to put tissue- and cell type-specific molecules into a functional context*.

This may probably be regarded as common aim for most of the journals which are chiefly devoted to histochemistry, but it is worth considering that peculiarities may also exist for each journal which essentially relate to its tradition. The subjects as well as the methods and techniques used in the recently published articles thus become an obvious filter for the authors in selecting the manuscripts to be submitted. As a consequence, the readership too is somewhat selected in a sort of self-propagating circle, which may become either virtuous or vicious for the future of a given journal.

No doubt, the primary goal of any journal is to extend its visibility and impact on the scientific community through the publication of high quality manuscripts; this may be reached by preferentially selecting the most appropriate hot-topics, excluding or reducing publica-

tion of papers on subjects whose interest is restricted to a relatively low number of scientists. However, a journal of histochemistry should also keep its role as a forum open to an audience as wide as possible, and this is especially appropriate for those small journals - such as the *European Journal of Histochemistry* - which are traditionally opened to an extensive choice of research topics. Presenting data on cell and tissue biology in a wide variety of models will help to increase our knowledge of the basic mechanisms governing development and differentiation under normal and pathological conditions; this will also help to increase the number of potential authors since scientists who generally do not use histochemistry in their research will find hints for the applications of histochemical techniques to novel and sometimes exclusive subjects. Of course, publishing articles on extremely specialized subjects realistically exposes a journal to the immediate risk of decreasing its impact factor, but this is a chance worth taking.

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