NRS Nuclear Receptor Signaling
An Open Access journal for the nuclear receptor signaling community

Nuclear Receptor Signaling: a home for nuclear receptor and coregulator signaling research

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The field of nuclear receptor and coregulator signaling has grown into one of the most active and interdisciplinary in eukaryotic biology. Papers in this field are spread widely across a vast number of journals, which complicates the task of investigators in keeping current with the literature in the field. In 2003, we launched Nuclear Receptor Signaling as an Open Access reviews, perspectives and methods journal for the nuclear receptor signaling field. Building on its success and impact on the community, we have added primary research and dataset articles to this list of article categories, and we now announce the re-launch of the journal this month. Here we will summarize the rationale that informed the creation and expansion of the journal, and discuss the possibilities for its future development.

Introduction

It has been almost five decades since the influence of gonadal steroids on de novo mRNA and protein synthesis was first demonstrated. These early experiments focused the mechanism of action of steroids on the nuclear DNA and paved the way for the identification and characterization of the nuclear receptor (NR) superfamily as the largest group of metazoan transcription factors, with broad physiological functions ranging from development and metabolism to the regulation of aging and neurological function. Beyond receptors, the discovery of orphan NR ligands and NR coregulator complexes has introduced the concept of an enormous structurally and functionally diverse group of molecules that is required for efficient activation or repression of gene expression by NRs. The field of nuclear receptor and coregulator signaling has grown into one of the most active and interdisciplinary in biology, with research communities spanning myriad basic disciplines including biochemistry, cell biology, chemistry, physiology, pharmacology, structural biology, medical subspecialties and informatics. Moreover, pre-clinical and clinical research into cancer, metabolic, reproductive, genetic and inflammatory diseases are fueling the development of drugs to bring the fruits of these research efforts to the bedside in the form of novel therapeutics.

Nuclear Receptor Signaling

One of the original mandates of the Nuclear Receptor Signaling Atlas (NURSA) Consortium was that it develop into a framework within which scientists from different disciplines, whose work related to NR signaling, could find common ground and potentially forge unanticipated collaborations. Consonant with this, we recognized that the field had matured and expanded to a point that justified the launch of a specialist title that could attract submissions with diverse scopes, and from different disciplines, into a single journal. Accordingly, after developing a journal platform entirely in house according to PubMed Central specifications, which was required for indexing in PubMed, we launched Nuclear Receptor Signaling (*NRS*) in 2003. Over the past decade or so, its reviews, perspectives and methods papers have furnished the field with insightful, authoritative Open Access articles encompassing multiple facets of NR and coregulator signaling.

A new paper category: primary research articles
Papers relevant to NR and coregulator signaling are widely distributed in a large number of journals. Articles published in 2012 matching the PubMed search terms “nuclear receptor” and “coactivator or corepressor”, for example, appeared in a total of 491 different journals! This is in one sense a corollary of the highly interdisciplinary nature of the field, and is not in itself necessarily a bad thing – these are all MEDLINE-indexed journals, after all. That said, the robust publication output of scientists active in these areas has seen a steady increase – some 40% over the past decade - in the number of publications per year. The sheer effort involved in keeping current with this information, not to mention varying experiences in terms of journal format, accessibility and focus, combine to make consumption of the research literature a less palatable exercise than it might otherwise be. Although this is a good problem to have, it is a problem nonetheless. The solution we propose, or at least a step towards it, is to begin publishing primary research articles in *NRS*.

With nearly 500 journals already publishing primary research related to nuclear receptors and coregulators, is there room for another? We believe there is, for the simple fact that none of these nearly 500 journals is dedicated solely to work across the entire NR field. We believe that *NRS* can fashion a niche for itself as a single, universally-accessible location for research in the field, tying together cutting-edge studies from the diverse disciplines in this field and facilitating the task of investigators in making insightful connections between these papers. Indeed, despite its focused number of article categories and modest article output to date, *NRS* has been a well-accessed and well-cited journal, a fact assisted no doubt by the fact that its content is freely available to the community. Moreover, we have hand-selected a geographically diverse editorial board of nearly 50 active scientists, ranging from seasoned senior investigators, to younger up-and-coming group leaders with already impressive research portfolios. Testament to the consensus in the community that *NRS* has been, and remains, an asset to our field, all but one of those scientists we reached out to recruit to the board accepted our invitation. Encouraged by this endorsement, we are pleased to announce that in addition to reviews and methods submissions, *NRS* is now accepting primary research manuscripts. Full details of the scope of the journal and information for authors can be accessed from the journal home page at www.nrsignaling.org.

Dataset Articles

Publication of primary research manuscripts is not the only new step for *NRS*. We will also accept submissions describing large, discovery-driven datasets. Recent years have seen a proliferation of datasets – expression microarray, RNA-Seq, ChIP-Seq, proteomic and metabolomic – affording us ever more intricate and finely-resolved perspectives on the mechanisms by which NRs, their ligands and coregulators modulate cell function. Given their complexity and the daunting weight of the information they contain however, such datasets are not of themselves readily embraced by the prevailing hypothesis-driven model of scientific publication. The net result has been that they are often used as a means to an end, with investigators selecting those data points most relevant to their hypothesis, and either consigning the rest to supplementary files, or not publishing them at all. As a consequence, these potentially valuable data resources are effectively hidden from view and are largely underused by the research community. The *NRS* Dataset Articles category will afford authors the opportunity to publish these datasets in full as independently-citable community research resources, with the proviso that they have emerged from a well-framed initial question and, naturally, that they meet the technical and scientific standards of peer review.

Diversity of *NRS* papers

The re-launch of *NRS* brings together a group of articles whose diversity augurs well for the future success of the journal in its mission of representing the myriad facets of the NR research community in a single forum. Highlighting the very current interest in the impact of dietary ligands on NR function, Benita Katzenellenbogen’s laboratory provides insight into estrogen receptor (ER) isoform-specific transcriptional effects of soy and licorice botanical ER ligands [Gong et al., 2014]. Lending credence to the hypothesis that signature cellular blends of coregulators might direct tissue-specific transcriptional compass of a given NR, Michael Stallcup’s group describes studies indicating that the presence or absence of specific coregulators gives rise to appreciable variations in glucocorticoid receptor-regulated transcriptomes in cultured cells [Wu et al., 2014]. In another of our re-launch articles, a review from Andrew Cato’s group discusses studies that cast molecular chaperones and cochaperones, such as p23 and Bag-1L, in roles beyond modulation of receptor-ligand interactions [Cato et al., 2014]. The high cost of drug development has propelled efforts to reposition existing approved drugs for other therapeutic endpoints, and an article from Paul Webb’s group describes a sequential screening platform for identifying novel selective ERβ (ESR2) agonists from libraries containing safe, off-patent compounds [Filgueira et al., 2014]. Finally, an article from Vincent Giguère’s laboratory extends previous studies by this group in challenging the conventionally-held role of retinoic acid receptor-β (RARβ/RARB) as a tumor suppressor, and in doing so, serves as a signal reminder of the context

specificity of NR and coregulator function [Liu and Giguère, 2014].

NRS and BD2K

Recognizing the importance of preserving large scale 'omics datasets for posterity, the National Institutes of Health is taking steps to modify its Public Access Policy to require deposition in public repositories of any such datasets supported by federal funds. Moreover, under the umbrella of its Big Data To Knowledge (BD2K) initiative, NIH has recently committed funds to building a dataset metadata repository – the Data Discovery index - that will allow researchers to discover NIH-funded datasets as conveniently as they do abstracts of published papers on PubMed, with the long term goal of increasing the accessibility and citability of these datasets. We believe that the informatics research community and scientific publishers can play a key collaborative role in transforming the way that researchers consume and leverage these resources to advance their own research efforts. As part of the NURSA project, we recently received BD2K funding to link the NURSA Transcriptomine database [Ochsner et al., 2012] with articles on journal websites, thereby allowing researchers to mine thousands of data points in a NR-related gene expression profiling dataset in a paper, to discover related data points in other articles, and to cite these datasets in their manuscripts and grant proposals. The ultimate goal is to demonstrate the feasibility and utility of providing readers of scientific articles with direct access to user-friendly data analysis tools that will facilitate their extraction and repurposing of useful information from those articles. Future editorials will announce the addition of this feature to *NRS* articles and keep readers apprised of its extension to other journals, and we welcome feedback from our readers on their experience using it.

Future directions

The success of *NRS* to date would not have been possible without the enthusiastic support of investigators in this field. *NRS* has been and will continue to be first and foremost a community-oriented journal, and we anticipate that it will forge an identity as a unique and important resource for primary research, reviews and techniques encompassing myriad aspects of nuclear receptor signaling. The concept of a journal that aspires to bring together in one place the best research on all biological, chemical, biophysical and clinical aspects of a specific family of transcription factors is, to our knowledge, unique in biology. Our ultimate goal is to provide our community with a focal point for the rich diversity of research and opinion that make this field what it is today.

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