

# Redox Scientific Literature Research

*By: Dr. Lee Ostler DDS, author "Redox Matters: Connecting the Dots Between Redox Biology and Health" and "Healthy Matters: Applying the Redox Lifestyle."*

The point of this exercise is to learn how to quickly navigate and move through multiple databases to search for any search term you are curious about. In practical application you will no doubt have multiple browser windows open simultaneously and will navigate back and forth as you read and learn.

Other information can be found from private websites, corporate-sponsored and education-based websites – all of which will add to your collective understanding of redox signaling and the Redoxome.

Why the emphasis on researching and searching primary sources related to redox science? Because secondary sources are few and far between about the science of applied redox biology! That is why I wrote "Redox Matters" and "Healthy Matters!" This is why I documented a combined 824 literature citations from the primary research databases in existence today, and put them in these books. No doubt the list could have been thousands. This article shows how that was done.

The point is that redox biology is well-documented in the literature. However, it is new enough that "redox" has not yet become a household, or common healthcare, term. But it soon will be. Count on it! But at this point there are no "therapies" or FDA approved treatments for disease at this point. I expect this will change in the future – as there are \$billions of dollars at stake for the development of redox-specific gene switches and therapies in the works. This will become very common and well known in the next decade or two. (I am aware of physicians now attending continuing education meetings who are being told that this is coming and they should begin to learn about it).

In the meantime, we can take advantage of becoming better informed and utilizing what is now available. None of us want to be, as a physician colleague recently said, "so open-minded that our brains fall out," but we also don't want to be that person who simply isn't aware. And as another physician pointed out to me recently, we may have hardening of our bodies (aging) happening, but we shouldn't let it happen in our brain! For those who have difficulty wrapping their minds around new and emerging science that affects their health or that of their patients (if they are health professionals), your mind should not be 'calcified!'

The invite here is to peel a few layers off this redox 'onion' and to discover what this is and where this is going. You may have to set aside some disbelief for a spell, to consider some of the ponderables. For doctors easily worried or even offended about information from sources other than their professional societies and the government, and who may ask why they haven't heard of this yet in their journals, consider that it takes 17 years – nearly 2 decades – before a new idea makes it into clinical practice. And then realize that those journals are now publishing this information, in abundance. Again – that is the purpose of this article – to show how this information is easily accessed by anyone with a computer, despite the fact that the textbooks are still (no doubt) being written.

Modern computer research tools enable access to vast libraries and databases of health-related information. The information sought should be carefully queried and even then, should be analyzed and cross-checked carefully. There are many reputable sources from which original information can be obtained and brought together. Redox signaling is not about therapy. It is about cellular health and prevention. To understand the latter, it is essential to have (at least) a rudimentary working knowledge of what redox biology is and how it works to keep cells healthy. Check out resources at [RedoxMatters.com](http://RedoxMatters.com), at [AmazingMolecules.net](http://AmazingMolecules.net), and other [private websites](#).

## Internet Research:

The following points may provide some guidance in how to conduct this level of research into the sophisticated reaches of specialized health information.

Any internet search engine is capable of fielding search inquiries by simply entering the search words and terms of interest. The search process and algorithms will return results that most relate to the terms entered in rank order of match or relevancy to the terms entered.

As a pattern of general research guidance for the novice, within the list of search engine results returned with a query, click and go into the articles presented. Some results will be commercially related and will promote specific products. Others will be editorial or commentary and opinion based, while other results will pull raw results directly from online research databases.

Some articles will reside behind a 'paywall' or subscription service. Don't be alarmed as sometimes you can find the same articles presented with other platforms in their entirety or by download or there will be other sites commenting about the article that can be informative.

For this level of health inquiry, give preference to original sources that pull from sites like PubMed.gov or from university research centers. This can be supplemented by other expert commentary that may help translate and communicate the findings given in the raw data of scientific literature.

All scientific articles are formatted similarly. They begin with title, author, and citation where the scientific paper is officially published. A credible science paper goes through many steps before being accepted for publishing. After the researchers and authors have performed their study, it is submitted to science journals for review and peer-review before it has been accepted. These checks and cross-checks help assure scientific validity in the design and execution of the said research project.

Within the science paper itself there are several sections and subsections worthy of attention. After the title and authors and citations are listed, a summary or abstract is then presented. These summaries generally fall within the *common use* provisions of copyright law, and therefore are almost always freely available. Many publicly available articles will proceed with the body of the science paper which include its introduction, the particulars of the science investigation or study, the discussion, and then a conclusion. Often many footnotes and cross-references are provided that link to related published research.

Focus first on the abstract of articles that are of interest. Note that most abstracts present a restatement of the known information about the topic at hand, a proposition or hypothesis to be tested, results of the study or experiment, a general discussion, and finally a conclusion and often suggestions for further research. One can gain much information and education from reading the abstracts to learn first what is known and already accepted as true, and then reading the conclusions. The research details are focused on study design, specific results and methodology, which are of more interest to other scientists and are usually of less interest to the 'amateur' researcher.

Internet search engines are a good place to start, as long as caution is used in selecting the specific articles returned in the query. Alternatively, one can directly access the PubMed.gov website and enter search terms there. PubMed, and NIH (National Institutes of Health) sites are trustworthy databases as far as accessing primary or original research. It will be up to you to determine the veracity of specific research. Remember that generally no one single article is enough to tell the whole story. By stitching together multiple abstracts and research papers,

a 'story' will begin to emerge that represents 'the truth' as derived from a preponderance of evidence. People writing about this science, and particularly those with a vested interest to protect or project, will make conclusions from specific papers, but more credibility is fostered when many cross-referenced and cross-checked articles are brought together that generally support the common thesis being studied.

It is also good to keep in mind the collective biases and 'leanings' within the framework of the topic matter studied. This relates to the presentation and discussion of research that represents varied ideologies for health care – some that may lean toward so-called modern medical intervention, or alternative medicine, or 'natural' medicine, or herbal medicine, etc.

As it relates to studying redox biology - if you are familiar with the nuances of science literature mentioned previously, this method of inquiry and study will be rewarding. Using this process, focus on the main points and highlights presented. You will at least come away with a sense of the legitimacy and place for redox biology and cell signaling in health processes.

In summary: By reading the introductions and the conclusions of many articles one can begin to piece together and appreciate the legitimacy of, and role of redox signaling in, any disease process investigated. Further study yields information about the deeper science of redox biology. To whatever depth it is taken, one can learn the principles of basic redox biology and the important role that redox signaling plays in cellular health.

#### **Computer Research Tip:**

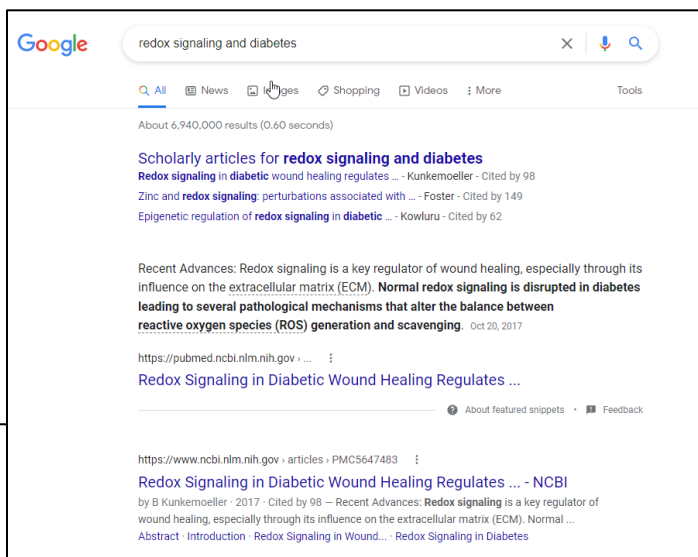
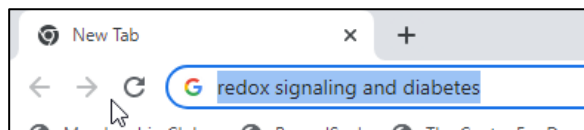
Most internet browser windows and pages allow you to search for specific words existing on the search results browser screen. Once an initial search term has been entered and results returned, search the displayed page for any specific word or phrase of interest. This allows you to quickly scan through an otherwise difficult research report in order to find the pertinent and specific words/comments where the particular word/phrase is located within the body of the report.

To do this, use any internet browser and perform a search query. From the search results, select a link leading to a specific research report on your topic of choice. Once you have navigated to the linked article or page, conduct a word/phrase search on that page using your internet browser search tool, to see where your chosen text is displayed within the body of the article.

For example, on any search results page returned, search for "redox," "redox signaling," "oxidation" or "oxidative stress" – or any word you are studying. (In the Google Chrome browser this is done with the "Alt-E-F" keys). Quickly scan the page by clicking on the arrows in the search box to move to the next location on the page the search word appears. Again, this is a quick way to scan through any article displayed on a screen (text or PDF) to find the occurrence of the topic or phrase buried deep in a given article.

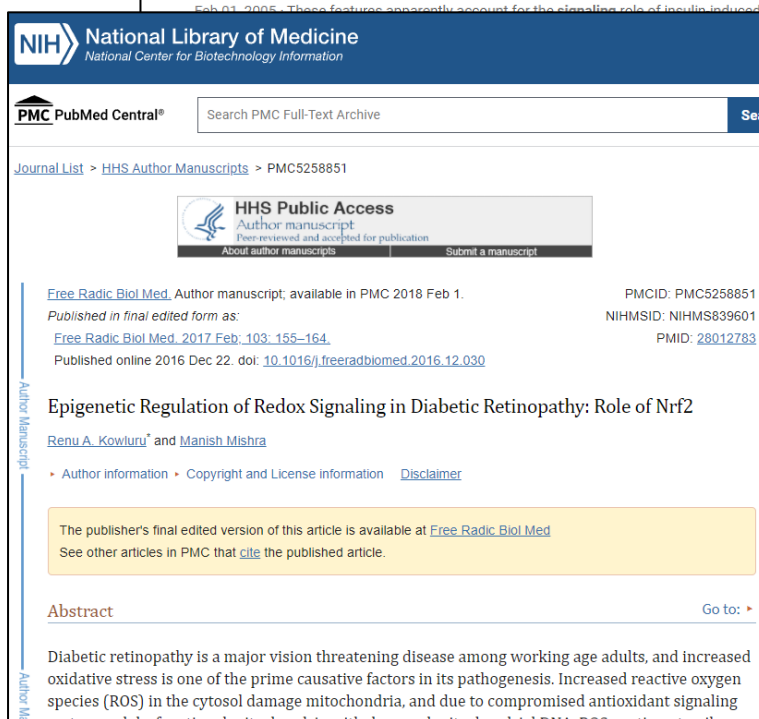
## Sample Redox Literature Search – Step-by-Step Example:

1. The topic of interest might be Redox Signaling and Diabetes. Using the Chrome browser type the search words “Redox Signaling and Diabetes” into the Chrome browser URL window. Press Enter to display these search results. Note that an alternative starting place can be in the pubmed.ncbi.nlm.nih.gov site itself (search for “Pubmed”), or within “Google Scholar”.
2. The search results will appear as follows on the particular day this was done. It will change from day to day and from browser to browser.
3. Scrolling down we find more articles:
4. Click on the article titled “Epigenetic Regulation of Redox Signaling in Diabetic...” (hint – right click on the link and open in a new browser tab/window. This makes it easy to go back to the original search and continue scrolling down the list to other related articles that were queried in the original search.)
5. Speed read the Abstract – especially the first 2-3 sentences and the last 2-3 sentences to search for and evaluate relevant information to your original search question. A quick roll of the mouse will reveal if the body of the article is present in this view, or simply the abstract. Also look for illustrations as they and their captions and descriptions often summarize and capsize relevant information quickly.



**Epigenetic Regulation of Redox Signaling in Diabetic ...**  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5258851>  
Diabetic milieu also alters epigenetic factors responsible for chromatin modifications and gene regulation, and kelch-like ECH-associated protein 1 (Keap1), important in regulating Nrf2 ...  
Author: Renu A. Kowluru, Manish Mishra Publish Year: 2017

**Redox Paradox | Diabetes | American Diabetes Association**  
[https://diabetesjournals.org/diabetes/article/54/2/...](https://diabetesjournals.org/diabetes/article/54/2/)



NIH National Library of Medicine  
National Center for Biotechnology Information

PMC PubMed Central® Search PMC Full-Text Archive

Journal List > HHS Author Manuscripts > PMC5258851

HHS Public Access  
Author manuscript  
Peer-reviewed and accepted for publication  
About author manuscripts Submit a manuscript

Free Radic Biol Med. Author manuscript; available in PMC 2018 Feb 1. PMID: PMC5258851  
Published in final edited form as:  
Free Radic Biol Med. 2017 Feb; 103: 155–164. NIHMSID: NIHMS839601  
Published online 2016 Dec 22. doi: 10.1016/j.freeradbiomed.2016.12.030 PMID: 28012783

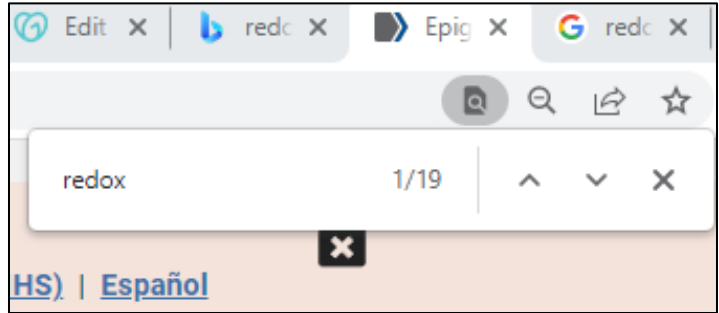
Epigenetic Regulation of Redox Signaling in Diabetic Retinopathy: Role of Nrf2  
Renu A. Kowluru\* and Manish Mishra  
• Author information • Copyright and License information • Disclaimer

The publisher's final edited version of this article is available at [Free Radic Biol Med](#)  
See other articles in PMC that [cite](#) the published article.

Abstract Go to: ▶

Diabetic retinopathy is a major vision threatening disease among working age adults, and increased oxidative stress is one of the prime causative factors in its pathogenesis. Increased reactive oxygen species (ROS) in the cytosol damage mitochondria, and due to compromised antioxidant signaling custom and dysfunctional mitochondria with damaged mitochondrial DNA, ROS continue to pile up

6. Begin a search on this page for relevant words specific to your interest. Sometimes these specific words are buried deep in the article and I want to find them quickly and read the few sentences before and after them to see what they can teach. To do this, (on a PC) click “Alt-E”, then “F”. This opens the browser search function in the upper-right of the screen. Type in the word you want to search for – in this case “redox”. In this search it yielded 19 instances of this word on this page – anywhere on the page (not just the article itself). It will generally default to highlighting the first instance of the word on the page, which in this case was the word “redox” in the article title.



7. Continue clicking on the up or down arrow in the browser search feature to advance to the next or previous instance of the word – and quickly scroll through the article looking for highlighted locations of the word. The third and fourth instance are highlighted and a quick read of the surrounding text show it discusses important features of how the Nrf2 transcription factor and its translocation to the nucleus following a redox signaling event, works. Note that the info in the illustration help establish the legitimacy of the Nrf2/Keap1 mediated signaling axis and its relationship with diabetes.

[Free Radic Biol Med. 2017 Feb; 103: 155–164.](#)  
 Published online 2016 Dec 22. doi: [10.1016/j.freeradbiomed.2016.](#)

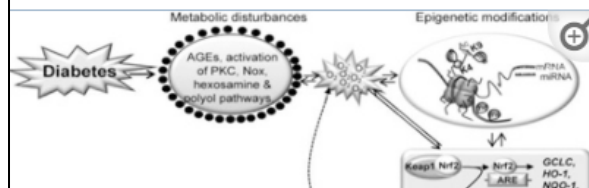
### Epigenetic Regulation of Redox Signaling in Diab

[Renu A. Kowluru\\*](#) and [Manish Mishra](#)

► [Author information](#) ► [Copyright and License information](#) [Disclaim](#)

regulating Nrf2-antioxidant signaling axis, is epigenetically modified, imped-  
 n of Nrf2, and this inhibits the transcription of genes with Antioxidant Redox  
 discusses antioxidant signaling, especially the role of Nrf2, in diabetic  
 e involvement of epigenetic modifications in antioxidant signaling and Nrf2  
 Therapies targeting Nrf2 activation, including epigenetic modifications,  
 drial damage and inhibit the development, and progression of this sight-  
 ch most of the patients get after 20–25 years of diabetes.

ropathy, epigenetic modifications, Nrf2, Redox signaling



8. Note that this information does not talk about a specific treatment or modality of care, but it does establish the reality of redox signaling biology and its relationship with this specific disease process.

9. Scrolling further down this page we fine the fifth and sixth instance. Note the bracketed numbers nearby which are hyperlinked to footnotes that provide an internet ‘wormhole’ to other articles. Clicking on

are considered to facilitate the recruitment of p65 subunit of transcription factor  
 noter; upregulating its gene transcription [92]. Furthermore, thio**redoxin** interact-  
 ndogenous inhibitor of antioxidant thio**redoxin**, is also shown to undergo epigenetic  
 diabetes [93].

IA methylation and histone modifications, many miRNAs also play a significant role  
 nt of diabetic retinopathy. Experimental models of diabetic retinopathy have sug

these numbers will take you to the footnotes and/or display the article title and link which you can access to proceed onward (again right-click so you can come back to the same tab and continue there).

10. This image shows the results of clicking on the #93 footnote and the pop-up window that appears, which can then be clicked on to take you to this article.

are considered to facilitate the recruitment of p65 subunit of transcription factor, upregulating its gene transcription [92]. Furthermore, thioredoxin is an endogenous inhibitor of antioxidant thioredoxin, is also shown to undergo epigenetic changes in diabetes [93].

93. Perrone L, Devi TS, Hosoya K, Terasaki T, Singh LP. Thioredoxin interacting protein (TXNIP) induces inflammation through chromatin modification in retinal capillary endothelial cells under diabetic conditions. *J Cell Physiol.* 2009;221:262-272. [PubMed] [Google Scholar] [Ref list]

A methylation of diabetic...  
 regulation of v...  
 195 and miR...  
 Ob is also cu...  
 ss-sectional case-control study from the EURODIAB Prospective Complication Study 1 diabetic patients has shown a strong association between miR-126 levels

11. Often – depending on the browser and the section of PubMed, or with other databases, there is a section in the sidebar area where there are links to “similar articles”. These are also possible rich ‘wormholes’ that can lead to additional information on the topic.

diabetic associated in the pathology have associated -9 (MMP-9) associated ation and encodes mi-

SHARE

RESOURCES

[Similar articles in PubMed](#)

12. If starting the process inside PubMed itself, a search of the same search terms shows the following: Note that there are 215 pages of results for this search. Also note at the bottom of the browser window there are 2,142 articles in these 215 pages.

The screenshot shows the PubMed.gov search results for the query "redox signaling and diabetes". The page header includes the NIH logo and the text "National Library of Medicine National Center for Biotechnology Information". The search bar contains the query "redox signaling and diabetes" and shows "2,142 results". The results are sorted by "Best match" and displayed on page 1 of 215. The first result is titled "Reactive oxygen species (ROS) homeostasis and redox regulation in cellular signaling." by Ray PD, Huang BW, Tsuji Y. The abstract snippet reads: "Oxidative stress results in macromolecular damage and is implicated in various disease states such as".

**Redox Signaling** from and to Peroxisomes: Progress, Challenges, and Prospects.  
 10 Fransen M, Lismont C.  
 Cite Antioxid Redox Signal. 2019 Jan 1;30(1):95-112. doi: 10.1089/ars.2018.7515. Epub 2018 Mar 22.  
 PMID: 29433327 Review.  
 Share Recent Advances: H(2)O(2) is an important **signaling** messenger that controls many cellular processes by modulating protein activity through cysteine **oxidation**. Somewhat surprisingly, the potential involvement of peroxisomes in H(2)O(2)-mediated **signaling** proce ...

---

2,142 results [Show more results](#)

---

« First < Prev Page **1** of 215 Next > Last »»

13. Clicking on the #1 article listed goes to this article – and the learning process continues...

Review > Cell Signal. 2012 May;24(5):981-90. doi: 10.1016/j.cellsig.2012.01.008.  
 Epub 2012 Jan 20.



## Reactive oxygen species (ROS) homeostasis and redox regulation in cellular signaling

Paul D Ray <sup>1</sup>, Bo-Wen Huang, Yoshiaki Tsuji




Affiliations + expand  
 PMID: 22286106 PMCID: PMC3454471 DOI: 10.1016/j.cellsig.2012.01.008  
[Free PMC article](#)

### Abstract

Reactive oxygen species (ROS) are generated during mitochondrial oxidative metabolism as well as in cellular response to xenobiotics, cytokines, and bacterial invasion. Oxidative stress refers to the imbalance due to excess ROS or oxidants over the capability of the cell to mount an effective antioxidant response. Oxidative stress results in macromolecular damage and is implicated in various disease states such as atherosclerosis, diabetes, cancer, neurodegeneration, and aging. Paradoxically, accumulating evidence indicates that ROS also serve as critical signaling molecules in cell proliferation and survival. While there is a large body of research demonstrating the general effect of oxidative stress on signaling pathways, less is known about the initial and direct regulation of signaling molecules by ROS, or what we term the "oxidative interface." Cellular ROS sensing and metabolism are tightly regulated by a variety of proteins involved in the redox (reduction/oxidation) mechanism. This review focuses on the molecular mechanisms through which ROS directly interact with critical signaling molecules to initiate signaling in a broad variety of cellular processes, such as proliferation and survival (MAP kinases, PI3 kinase, PTEN, and protein tyrosine phosphatases), ROS homeostasis and antioxidant gene regulation (thioredoxin, peroxiredoxin, Ref-1, and Nrf-2), mitochondrial oxidative stress, apoptosis, and aging (p66Shc), iron homeostasis through iron-sulfur cluster proteins (IRE-IRP), and ATM-regulated DNA damage response.

FULL TEXT LINKS  
  


ACTIONS  
[Cite](#)  
[Favorites](#)

SHARE  
  
  


PAGE NAVIGATION  
 < Title & authors  
 Abstract  
 Figures  
 Similar articles  
 Cited by  
 Publication types