Obtaining Scientific Information

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Scientific or Medical Literature Information

- They are classified into:
 - Primary: Original research & analysis
 - <u>Secondary</u>: No interpretation, just helps you find sources
 - <u>Tertiary:</u> Interpretation of primary data
- Information must be:
 - Current: Up to date
 - <u>Critically examined</u>: Reviewed, more than one resource,.....
 - <u>Relevant and specific:</u> As related to the subject of interest

Primary Resources

Ex. Journals Original articles, NOT Review articles

Benefits:

- 1. Up to date and keep up with new advances/development
- 2. Enhance communications and share opinions with other healthcare professionals
- 3. Obtain continuing education

Limitations:

 Although publication of an article is well known, respected journal enhances the credibility of information contained in an article, this does not guarantee that the article is accurate.

Secondary Resources

Ex.: Indexing and abstracting services

Benefits:

Valuable tools for quick and selective screening of the primary literature for specific information, data, citation, and articles.

Examples:

PubMed; Google Scholar; Scopus; Ovid; Web of Science; Embase; Cochrane Library; OpenMD; Pharmaceutical News Index; International Pharmaceutical Abstracts; ClinAlert;

Limitations:

- May not contain all articles
- Lag time (*i*.e., the interval between the publication of an article and the citation of that article in an index).
- May require subscription

> Tertiary Resources

Ex.: Textbooks

Benefits:

- Provide easy and convenient access to a broad spectrum of related topics
- Background information on drugs and diseases is often available.

Limitations:

- 1) Not recent, it could take several years to publish a text book
- 2) The author of a textbook might not have conducted a thorough search of the literature.

> Tertiary Resources

Ex. : Databases and Internet

Benefits:

- Convenient, easy to use, and referenced.
- Similar to textbooks, but updated more frequently.
- Useful resources for drug monographs, pill identifications, drug interactions, and various therapeutic calculations
- Information must be obtained only from accredited/peer-reviewed known websites

Limitations:

- Lag time, my not as complete, depends on author interpretation
- May require subscription

Examples:

Micromedex, Lexi-Comp, UptoDate, NICE.org.uk, NHS.org.uk, FDA.gov, CDC.gov, Guideline.gov, clinicaltrials.gov, Mayo.edu, Medscape.com, Emedicine.com, Drugs.com, Rxlist.com, Druginfo.com, Cancer.gov, NIH.gov, Webmed.com,, PDR.com, AHFS, PDR, USP Drug Information, Drug Facts and Comparisons, Martindale: The Complete Drug Reference.

Note:

Several databases are available as mobile apps.



Most Current:



Searching Tips

<u>Use specific keywords:</u>

- Ex: Inflammation, acute kidney injury (AKI), liver, fibrosis, cytokines, interleukins, oxidative, hepatic stellate cell, TGF,
- Avoid common words (a, an, the.....) and punctuation
- Use root of word ex: decrease not decreasing

Search all related terms:

- Ex: oxidative/redox/antioxidant/glutathione/SH/NADPH oxidase (NOX).....
- Inflammation/cytokines/interleukines/
- liver/hepatic/biliary/NAFLD/NASH/HCC/HBV/HCV.....
- insulin/diabetes/obesity/hyperglycemia/GLUT-4/GLUT-2......
- kidney/renal/glomerular/proteinuria/AKI/CKI/.....
- Heart/arrhythmia/dysrhythmia/bradycardia/tachycardia/CK-MB/cTnI/cardiac output....

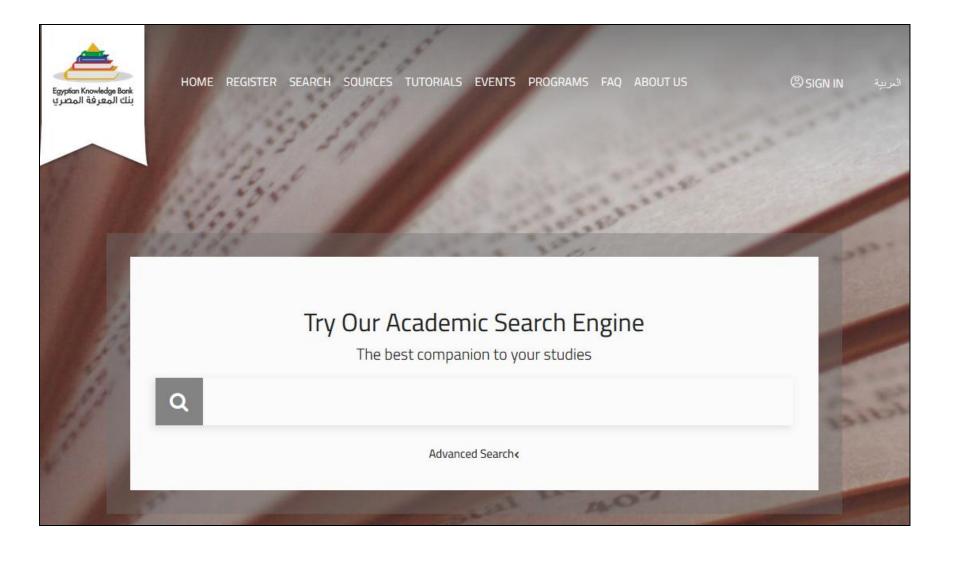
Take care of variants:

- Ex: hyperten* for both hypertension and hypertensive;
- diabet*;
- oxidati*;
- Inflammat*;

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Assay Kits ELISA Kit Search, ELISA Kits	Histochemistry / IHC	Protein Biochemistry Proteomic Tools, Western Blotting	Assay Kits
Biomolecules	Lab Automation	Gene Expression	
Proteins, Peptides, Enzymes	Dispensers, Washers, Handlers	qPCR, Microarrays, RNAi, RNA-Seq	Cells & Microorganisms
Bio-Imaging / Microscopy Gel Imaging, Microscopes	Lab Equipment Shakers, Refrigeration, Imaging	Services Antibody Services, Peptide Synthesis	Custom Antibody Services
Cell Biology	Cell / Tissue Culture	Translational Research	Flow Cytometers
Cell Analysis, Cytometers, Cell Counters	Media, Cells, Culturing Equipment	In Vivo Imaging, Live Cell Imaging	
Molecular Diagnostics	Drug Discovery and Development	Chromatography	Thermal Cyclers
Infectious Agents, qPCR Assays	Drug Screening, Bioprocessing	Chromatography Search Tool	Microscopes / Cell Imagers
Single Cell Analysis Single Cell Sequencing, Cell Isolation	Flow Cytometry Flow Cytometers, Flow Antibodies	Next Gen Sequencing NGS Kits, Library Prep	Microplate Readers
Spatial Biology	Cell-Based Assays	Spectroscopy	Gel Imaging Systems
Spatial Biology Platforms	Cell Viability, Apoptosis Assays	Specs, Mass Spec, Plate Readers	Get maging systems

≻ <u>What is your aim?</u>

- What is your specific target? (treatment, prevention, decrease complications,...)
- Is it acute or chronic?
- Are current therapies not sufficient? What is missing/disadvantages?
- What is the main advantage(s) your aim will add to current situation?
- Always look for the current and future treatments if available for your disease

≻ <u>Example:</u>

- Insulin Resistance
- Liver Fibrosis
- Acute inflammation
- Acute kidney injury

-

Choosing your model?

- Clinical or Experimental?
- What research animal is suitable and resemble human disease model?
 - Ex. Can rodents be used for dyslipidemia/atherosclerosis?
- How to induce the disease or the dysfunction?
 - Ex. Chemical , surgical, genetic,
- What is the shortcomings of the model compared to other models?
 - Ex. LPS vs CLP; thioacetamide vs BDL; Bleomycin-induced lung fibrosis injection vs Intratracheal
- Availability
- Duration
- Cost

Choosing your pathway?

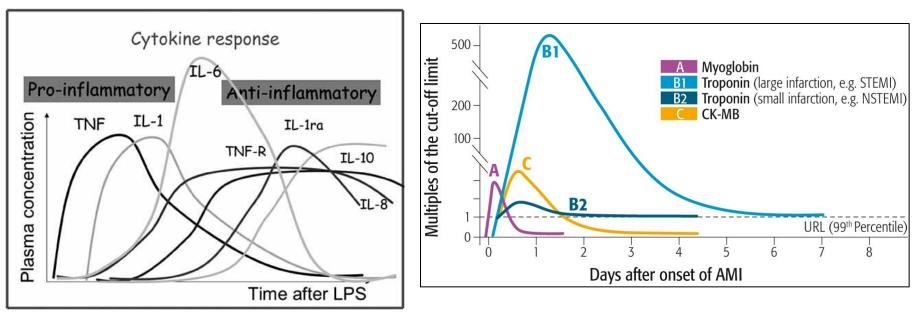
- What are the possible pathways/mechanisms that can treat or prevent this disease or its complications?
- See what pathway your intervention (Ex. Drug) can specifically affect
- Try to follow this pathway using key biomarkers, be specific.
- Can you measure this pathway markers? Are they available? What alternatives?
- Examples

Choosing your biomarkers?

- Always check that your model already express biomarkers for the disease? And which ones will your intervention affect?
 - Ex. <u>Insulin resistance</u>: HOMA-IR, TGs, Insulin, glucose, GLUT-4, HB_{A1C}, <u>New Biomarkers</u>
 - <u>Liver fibrosis</u>: α-SMA, Masson's trichrome stain, TGF-β1, PDGF, TIMP-1, TIMP-2, MMP-2, adeponectin, leptin, <u>New Biomarkers</u>.....
 - <u>Acute kidney injury</u>: Cystatin-c, KIM-1, NGAL, microalbuminuria, creatinine clearance, GFR, <u>New Biomarkers</u>.....
 - <u>Acute inflammation:</u> IL-1, IL-6, IL-13, IL-10, TNF-α, CRP, <u>New</u> <u>Biomarkers</u>.....
 - <u>Oxidative stress:</u> Total antioxidant, Lipids (MDA, isoprostanes, oxLDL, ...), Proteins (nitrotyrosine, carbonyl assay,), DNA (DNA breaks, 8-OHdG,), NOX, <u>New Biomarkers</u>.....
 - <u>Apoptosis:</u> Tunnel assay, Annexin V, BAX/BCL2, Caspase-3, <u>New</u> <u>Biomarkers</u>.....

Choosing your biomarkers?

- <u>Can you measure these biomarkers? What method is better?</u>
 - Ex. <u>NFκB regulation</u> is through translocation to nucleus not by changing expression
 - <u>Measure activity</u> (Ex. Phosphorylation by WB), <u>protein expression</u> (ELISA, WB), <u>mRNA expression</u> (real time PCR),
- <u>Is there a specific profile/time frame to measure these biomarkers?</u>





Insulin Resistance: From Mechanisms to Therapeutic Strategies

Shin-Hae Lee¹, Shi-Young Park¹, Cheol Soo Choi^{1,2,3}



REVIEW ARTICLE OPEN Targeting fibrosis: mechanisms and clinical trials

Manyu Zhao¹, Liqun Wang¹, Mengzhu Wang¹, Shijie Zhou², Ying Lu², Huijie Cui¹, Alexandra C. Racanelli^{3,4}, Ling Zhang⁵, Tinghong Ye p^2 , Bisen Ding p^6 , Ben Zhang¹, Jinliang Yang^{2 \bowtie} and Yuqin Yao $p^{1,2<math>\bowtie}$

Fibrosis is characterized by the excessive extracellular matrix deposition due to dysregulated wound and connective tissue repair response. Multiple organs can develop fibrosis, including the liver, kidney, heart, and lung. Fibrosis such as liver cirrhosis, idiopathic pulmonary fibrosis, and cystic fibrosis caused substantial disease burden. Persistent abnormal activation of myofibroblasts mediated by various signals, such as transforming growth factor, platelet-derived growth factor, and fibroblast growh factor, has been recongized as a major event in the occurrence and progression of fibrosis. Although the mechanisms driving organ-specific fibrosis have not been fully elucidated, drugs targeting these identified aberrant signals have achieved potent anti-fibrotic efficacy in clinical trials. In this review, we briefly introduce the aetiology and epidemiology of several fibrosis diseases, including liver fibrosis, kidney fibrosis, cardiac fibrosis, and pulmonary fibrosis. Then, we summarise the abnormal cells (epithelial cells, endothelial cells, immune cells, and fibroblasts) and their interactions in fibrosis. In addition, we also focus on the aberrant signaling pathways and therapeutic targets that regulate myofibroblast activation, extracellular matrix cross-linking, metabolism, and inflammation in fibrosis. Finally, we discuss the anti-fibrotic drugs based on their targets and clinical trials. This review provides reference for further research on fibrosis mechanism, drug development, and clinical trials.

Signal Transduction and Targeted Therapy (2022)7:206

; https://doi.org/10.1038/s41392-022-01070-3



CRITICAL REVIEWS IN CLINICAL LABORATORY SCIENCES https://doi.org/10.1080/10408363.2021.1879000



Check for updates

REVIEW ARTICLE

Current concepts and advances in biomarkers of acute kidney injury

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International Journal of *Molecular Sciences*



Review

Biomarkers and Mechanisms of Oxidative Stress—Last 20 Years of Research with an Emphasis on Kidney Damage and Renal Transplantation

Karol Tejchman ¹, Katarzyna Kotfis ²,*¹ and Jerzy Sieńko ¹



