

**Ovarian Bioinformatics and Research Strategies**

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Stanford University  
USA

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**Ovarian Bioinformatics and Research Strategies**

**Selection of Research Topics:**

**Experimentation:**

**Manuscript Preparation:**

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**Strategies in Ovarian Research**

**Selection of research topics:**

**-Literature survey (PubMed, Google, Google Scholar, ClusterMed)**

Google Scholar [Web](#) [Images](#) [Video](#) [News](#) [Maps](#) [more »](#)

ovarian follicle   [Advanced Scholar Search](#)  
[Scholar Preferences](#)  
[Scholar Help](#)

**Scholar** All articles - [Recent articles](#) Results 1 - 10 of about 83,500 for ovarian follicle [definition]. (0.54 sec)

**Follicle stimulating hormone is required for ovarian follicle maturation but not male fertility** - [Find it@Stanford](#)  
[Find It @ Stanford Med](#) - all 4 versions »  
TR Kumar, Y Wang, N Lu, MM Matzuk - Nature Genetics, 1997 - nature.com  
... Nature Genetics 15, 201 - 204 (1997) doi:10.1038/ng0297-201 Follicle stimulating hormone is required for ovarian follicle maturation but not male fertility. ...  
[Cited by 481](#) - [Related Articles](#) - [Web Search](#) - [BL Direct](#)

**Ovarian follicle atresia: a hormonally controlled apoptotic process** - [Find it@Stanford](#) - [Find It @ Stanford Med](#)  
all 3 versions »  
AJ Hsueh, H Billig, A Tsafiri - Endocr Rev, 1994 - ncbi.nlm.nih.gov  
Endocr Rev. 1994 Dec;15(6):707-24. Click here to read **Ovarian follicle atresia: a hormonally controlled apoptotic process**. Hsueh ...  
[Cited by 353](#) - [Related Articles](#) - [Web Search](#) - [BL Direct](#)

**Growth differentiation factor-9 is required during early ovarian folliculogenesis** - [Find it@Stanford](#) - [Find It @ Stanford Med](#) - all 5 versions »  
J Dong, DF Albertini, K Nishimori, TR Kumar, N Lu, ... - Nature, 1996 - ncbi.nlm.nih.gov  
... GDF-9, which is required for ovarian folliculogenesis. GDF-9 messenger RNA is synthesized only in the oocyte from the primary one-layer follicle stage until ...  
[Cited by 409](#) - [Related Articles](#) - [Web Search](#) - [BL Direct](#)

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## Strategies in Ovarian Research

### Selection of research topics:

-Literature survey (PubMed, Google, Google Scholar, ClusterMed)

granulosa cell 250 results Search PubMed

Top 250 results of at least 11,000 retrieved for the query granulosa cell (Details) (View at PubMed)

Select/deselect all on this page Selected results: 0 View Email Export Text

- Volker HJ, Engert S, Cramer A, Schmidt M, Kammerer U, Muller-Hermelink HK, Gattenlohner S [new window] [cluster] [filter view] **Expression of CD56 isoforms in primary and relapsed adult granulosa cell tumors of the ovary.** Diagn Pathol. 2008 Jul 9;3(1):29. [Epub ahead of print].  
[.] length (CD56140/180kDa). The reaction was assessed with respect to percentage of positive and intensity of staining. RESULTS: In all GCTs, CD56Pan was expressed, but differences were [.]
- Fan HY, Liu Z, Cahill N, Richards JS [new window] [cluster] [filter view] **Targeted Disruption of Pten in Ovarian Granulosa Cells Enhances Ovulation and Extends Life Span of Luteal Cells.** Molecular Endocrinology. 2008 Jul 7 [Epub ahead of print].  
FSH activates the PI3K/AKT pathway and thereby enhances granulosa cell differentiation in cult. To identify the physiological role of the PI3K pathway in vivo we disrupted the PI3K [.]
- Matsuda F, Inoue N, Goto Y, Maeda A, Cheng Y, Sakamaki K, Manabe N [new window] [cluster] [filter view] **cFLIP Regulates Death Receptor-mediated Apoptosis in an Ovarian Granulosa Cell Line by Inhibiting Procaspase-8 Cleavage.** J Reprod Dev. 2008 Jul 7 [Epub ahead of print].

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## Strategies in Ovarian Research

### Selection of research topics:

-Literature survey (PubMed, Google, Google Scholar, ClusterMed)

-From one animal model to another (taking advantage of the human model)

-New technical approaches (e.g. RNAi, conditional knock out mice, new reagents)

-Advances in genome sequencing and DNA microarrays (Bioinformatic approaches; 20,000 human and mouse genes, DNA Microarrays and Gene Databases)

-From expression to functions

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**OKdb**

**THE OVARIAN KALEIDOSCOPE DATABASE**

- A website to serve the ovarian research community – (<http://ovary.stanford.edu>)

~2800 individual gene pages  
20-30 distinct users/day since 2001

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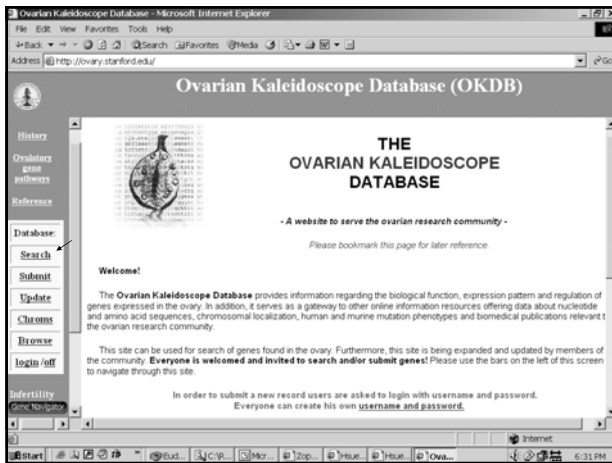
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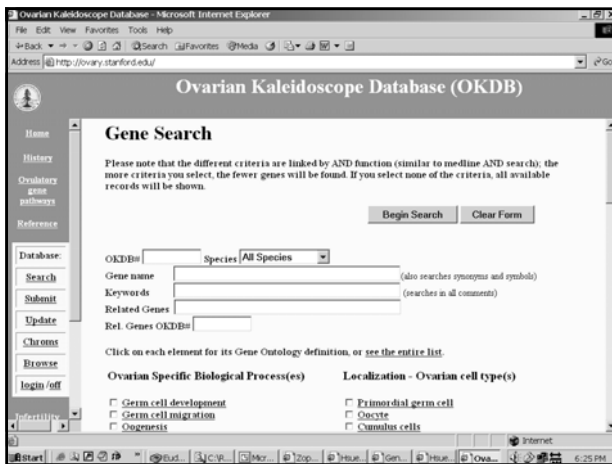
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**Bioinformatic Approaches in Ovarian Research**

**-From expression to functions (Bioinformatic approaches; DNA Microarrays and Gene Databases)**  
***OKdb (Ovarian Kaleidoscope Database)***  
**-Gene navigator**

**SEARCH for**  
**-FSHR, GDF9**

**-oocyte ligand, cell-type specific, mutation,**

**-hormone/oocyte, sequential,**

**-ligand-receptor, oocyte hormones on cytoplasmic maturation, luteal cells/steroidogenesis/receptor subtypes**

**-Infertility, subfertility, Chromosomal X, POF, Chromosome, Browse**

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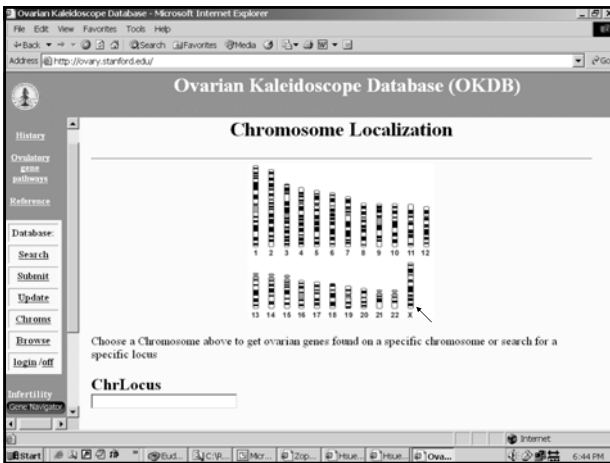
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**Bioinformatic Approaches in Ovarian Research**

**-From expression to functions (Bioinformatic approaches; DNA Microarrays and Gene Databases)**

*KEGG pathway, (apoptosis, TGFb pathway, etc.)*

*DNA array, early embryo arrays, preovulatory ovary arrays, BDNF as an example*

*log in, hsuehlab and labexpression*

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**The Human Genome Project (2001)**

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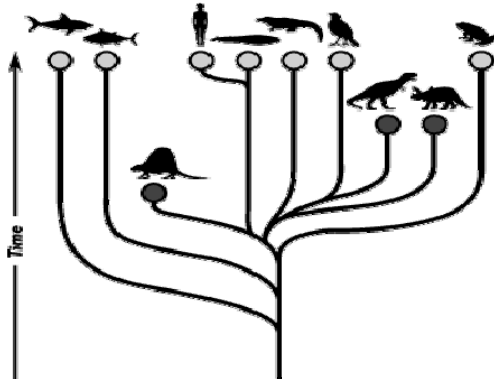
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**Phylogeny: In search of a common ancestor**




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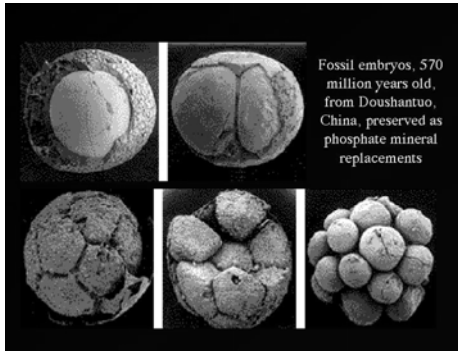
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**Genes expressed in early embryos are highly conserved during evolution**



Fossil embryos, 570 million years old, from Doushantuo, China, preserved as phosphate mineral replacements

Jun-Yuan Chen et al PNAS USA. 2000 97(9): 4457.

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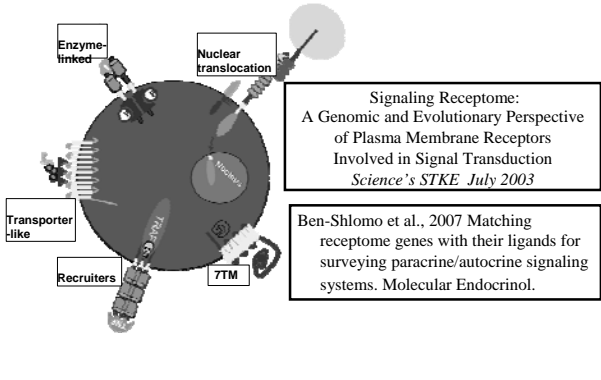
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**Human Plasma Membrane Receptome**

<http://Receptome.Stanford.edu>



Signaling Receptome: A Genomic and Evolutionary Perspective of Plasma Membrane Receptors Involved in Signal Transduction *Science's STKE July 2003*

Ben-Shlomo et al., 2007 Matching receptome genes with their ligands for surveying paracrine/autocrine signaling systems. *Molecular Endocrinol.*

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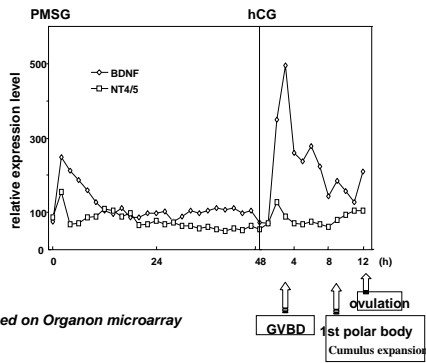
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**DNA microarray analyses of ovarian transcripts**

**Expression of BDNF and NT-4/5 during ovulation induction**




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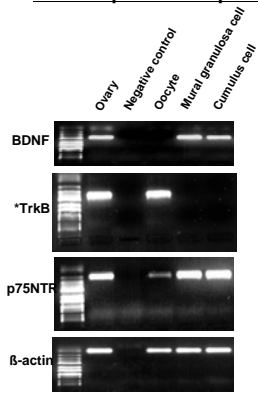
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**Ovarian Cell types expressing BDNF, TrkB, and the p75 coreceptor**

**Nested RT-PCR**




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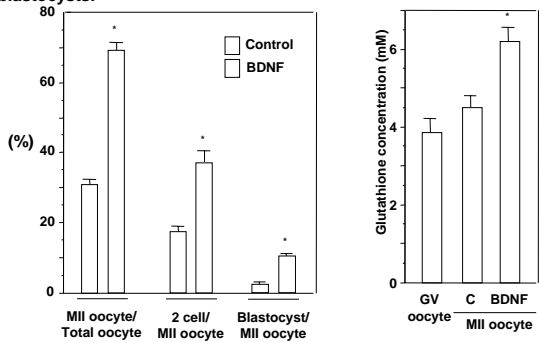
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**Effect of BDNF on oocyte progression to blastocysts**

Preovulatory oocytes from PMSG-treated mice were cultured for 16h with BDNF to allow first polar extrusion (MII), fertilized, and cultured for 5 days to blastocysts.




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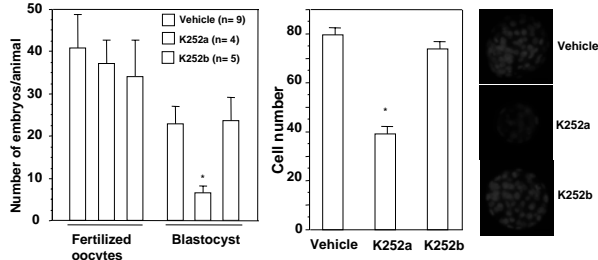
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**Effects of Trk inhibitor treatment on the development of preimplantation embryos in vivo**

Mice were treated with PMSG, followed by hCG with or without K252a, and mated. Zygotes were obtained from mice 22h later, and cultured for 5 days up to the blastocyst stage.




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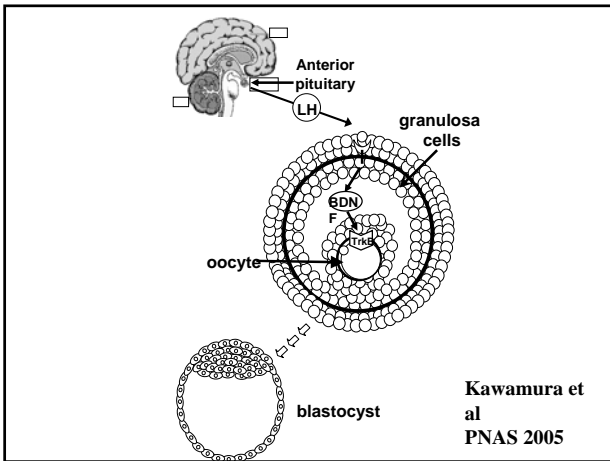
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**Genome-wide searches for autocrine systems during early embryonic development**

Microarray datasets (Wang QT, et al Dev Cell 2004) showed transcript levels for 12 stages from oocyte to blastocysts in mice.

GV (germinal vesicle), MII (first polar body extrusion), Zygote,

E2c (early two-cell), M2c (middle two-cell), L2c (late two-cell), 4c (four-cell), 8c (eight-cell), 16c (sixteen-cell),

Ebl (Early blastocyst), Mbl (Middle blastocyst), Lbl (Late blastocyst).

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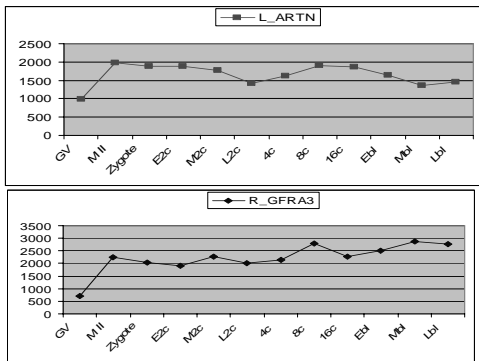
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**Expression of artemin (ARTN) and its receptor GFRA3 in mouse early embryos**




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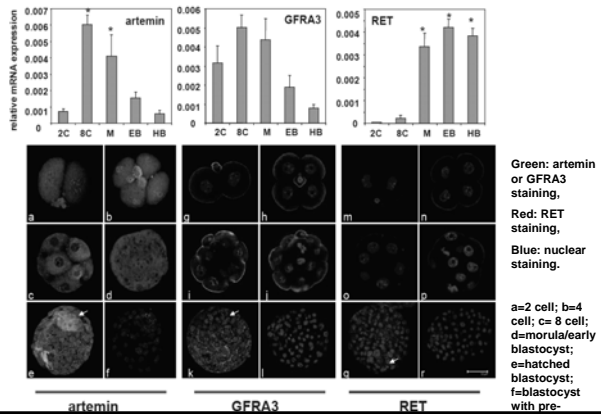
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**Expression of artemin, GFRA3 and RET proteins during preimplantation embryo development**




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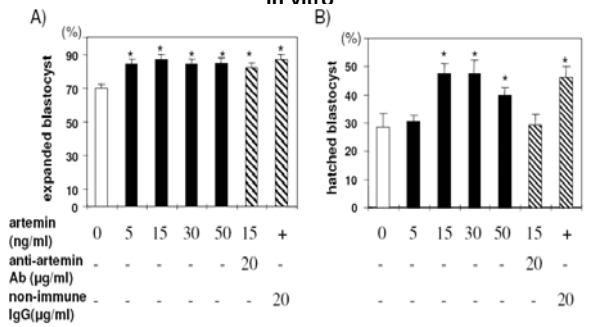
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**Effects of artemin on preimplantation embryo development in vitro**



Two-cell embryos treated with artemin showed increased blastocyst expansion (A, 72h) and hatching (B, 96h). The artemin effect was blocked by artemin antibodies.

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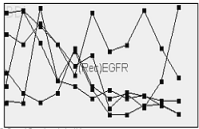
Human Plasma Membrane Receptome Search  or


Receptor Family  
RTK < ERBB/EGF

**Pre-computed DNA microarray datasets**

MAIN | RECEPTORS | INTERACTIONS | **NEW DNA MICROARRAY DATA**

Experiment: **Mm\_Testis\_Development** | 4 Receptors  
 Description: **Testes of mice at days 0, 3, 6, 8, 10, 14, 18, 20, 30, 35, and 56 of age.** read more.. see fields..

EGFR  

 0 Found 5 proteins for this gene.  
 Proteins are NOT to scale relative to each other.

ERBB2  

 0 Found 5 proteins for this gene.  
 Proteins are NOT to scale relative to each other.

Other experiments:  
 EmbryonicOvary  
 PituitaryAdenoma  
 PreimplantMmEmbryo

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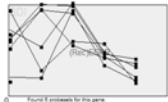
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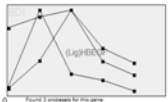
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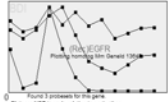
**Pre-computed DNA microarray datasets**

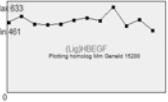
**Pituitary adenoma subtype**  
 Normal pituitary, pituitary adenomas secreting GH, PRL, or ACTH, and non-functioning adenoma. read more.. see fields..


 (Rec) EGFR

Interacts With  

 (Lig) HBEGF (Select Interactant)

**Preimplantation mouse embryo**  
 Selected stages: GV, mII oocyte, 2-cell, 4-cell, 8-cell, 16-cell and blastocyte. read more.. see fields..


 (Rec) EGFR

Interacts With  

 (Lig) HBEGF (Select Interactant)

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**Strategies in Ovarian Research**

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- From one model to another (taking advantage of the human model)
- New technical approaches
- From expression to functions (Bioinformatic approaches)

-Scientific fashion vs new paradigm

-Physiological findings vs pharmacological results (importance of endogenous actions)

-Applied research vs. pure research

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### Image Data Integrity and Standards

No specific feature within an image may be enhanced, obscured, moved, removed, or introduced.

Adjustments of brightness, contrast, or color balance are acceptable if they are applied to the entire image and as long as they do not obscure, eliminate, or misrepresent any information present in the original.

The grouping of images from different parts of the same gel, or from different gels, fields, or exposures must be made explicit by the arrangement of the figure (e.g., dividing lines) and in the figure legend.

Deviations from these guidelines will be considered as potential ethical violations. Authors should be aware that they must provide original images when requested to do so.

*Molecular Endocrinology* has begun beta testing RIGOUR, a new product being used by Cadmus Communications. Randomly selected manuscripts accepted for publication will undergo image integrity analysis to determine whether figures have been manipulated using techniques such as image deletion, image duplication, and healing brush tool application.

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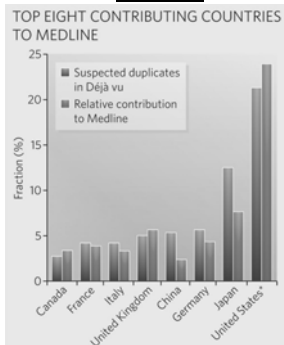
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### Using ETBlast Searches to Identify Duplicated Articles



Déjà vu Database: A study of scientific publication ethics.

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### Preparation of Manuscripts for Biomedical Journals

#### Scientific writing: clarity of the thinking process is more important than English writing

Original discoveries (or using new techniques) of major importance to different fields

Important discoveries to a particular field of research (or using a new experimental approach)

Expansion and confirmation of existing knowledge (or accumulation of knowledge, from quantitative to qualitative changes)

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**Good luck**  
**on your research projects and**  
**manuscript submission!**

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