# How can single-cell transcriptomic analysis reveal immune ev...

Question: How can single-cell transcriptomic analysis reveal immune evasion mechanisms and cell populations associated with relapse in solid tumors?

## 📄 Overview

🔍 Applying searching strategies...

📋 **Screening Results**

↳ Database: Europe PMC

↳ Search query: (single-cell RNA sequencing OR scRNA-seq OR single-cell transcriptomics) AND (immune evasion OR immune escape OR immunosuppression) AND (tumor relapse OR cancer recurrence OR disease relapse) AND (solid tumor OR solid tumour) AND (cell population OR cell cluster OR immune cell OR tumor microenvironment)

↳ Total identified: 838

↳ After relevance screening: 20

↳ Excluded: 818

⚠️ This report is based on Europe PMC abstract-level screening. Full-text screening requires institutional access and must be completed by the user. The full-text assessment stage of the PRISMA flow chart is not included in this output.

✅ Analyzed 838 studies · Synthesized the top 20

↳ Ranked by KlastroHeron using publicly available relevance criteria

↳ Citation impact: 🏆 Top 1%, 🥇 Top 5%, 🥈 Top 10% displayed

↳ Excluded 818 studies with lower relevance

✅ Found 20 papers. Analyzing...

## Evidence

**Research Evidence**:

• **Single-cell RNA sequencing (scRNA-seq) for tumor microenvironment (TME) deconstruction**: A review on endometrial carcinoma highlights how scRNA-seq and spatial transcriptomics (ST) enable the identification of distinct cell populations within the TME, including rare resistant subpopulations that conventional bulk sequencing obscures. These technologies allow the characterization of immune cell states associated with treatment response and relapse. DOI: https://doi.org/10.3389/fonc.2025.1685565

• **Computational single-cell frameworks for drug resistance and immune evasion**: A review integrating deep transfer learning with single-cell data (tools such as scDEAL and SCAD) demonstrates how pharmacological knowledge can be transferred from cell line data to clinical single-cell datasets, enabling the identification of rare but lethal drug-resistant subpopulations that drive relapse. Traditional population-averaged signals mask these subclones, underscoring the unique power of single-cell resolution in mapping immune evasion trajectories. DOI: https://doi.org/10.3389/fphar.2026.1786561

• **Immune evasion mechanisms in the tumor immune microenvironment**: The pan-tumor review on EBV-associated malignancies systematically describes convergent immune evasion strategies — including HLA modulation, steric immune blockade, and NF-κB/PI3K-AKT signaling — that can be dissected at single-cell resolution. These mechanisms are broadly relevant to solid tumors and represent key targets identifiable through transcriptomic profiling. DOI: https://doi.org/10.3389/fimmu.2026.1791347

• **Tumor evolution and clonal dynamics underlying relapse**: A Darwinian perspective on tumor evolution describes how genetic mutations, gene expression changes, and immune system interactions drive the selection of aggressive subclones capable of therapy resistance and metastasis. Single-cell transcriptomics is particularly suited to capturing this clonal heterogeneity and tracking evolutionary trajectories associated with relapse. DOI: https://doi.org/10.7150/ijbs.130014

• **Multi-omics and spatiotemporal technologies in precision oncology**: A review on thyroid cancer precision oncology discusses how multi-omics biomarkers and spatiotemporal technologies — including scRNA-seq — contribute to understanding tumor heterogeneity, radioiodine resistance, and the molecular taxonomy of aggressive variants, providing a framework applicable to immune evasion studies in solid tumors broadly. DOI: https://doi.org/10.2147/ijgm.s602509

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## 💡 Implications

**Clinical Implications**:

• This report may support literature review, clinical education, and professional reference, but it does not replace patient-specific clinical judgment.

• **Identification of immune-excluded and exhausted T-cell populations**: scRNA-seq enables the resolution of T-cell exhaustion states (e.g., $TOX^+$, $PD\text{-}1^+$ subsets) and immune-excluded phenotypes within the TME, which are directly linked to immune evasion and poor prognosis in solid tumors.

• **Detection of rare relapse-driving subpopulations**: Computational frameworks applied to single-cell data can identify minimal residual disease-associated or therapy-resistant cell states that are invisible to bulk transcriptomics, offering actionable targets for preventing relapse.

• **Spatial context matters**: Combining scRNA-seq with spatial transcriptomics allows researchers to map where immune-evasive interactions occur within the tumor architecture, distinguishing tumor core from invasive margin dynamics.

• **Therapeutic target discovery**: Immune evasion mechanisms identified at single-cell resolution — such as HLA downregulation, checkpoint ligand upregulation (PD-L1, CD47), and immunosuppressive cytokine secretion — can directly inform the rational design of combination immunotherapy strategies.

• **Monitoring clonal evolution**: Longitudinal single-cell profiling of pre-treatment and relapsed tumor samples can reveal the transcriptional reprogramming events that enable immune escape and clonal outgrowth, supporting the development of predictive biomarkers.

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## ⚠️ Limitations

**Study Limitations**:

• Several of the reviewed papers are narrative or systematic reviews rather than original single-cell studies, meaning primary scRNA-seq datasets and statistical power assessments are not directly evaluable from the available abstracts.

• The computational transfer learning frameworks (scDEAL, SCAD) described rely on cell line-derived pharmacological data, which may not fully recapitulate the complexity of the in vivo tumor immune microenvironment in solid tumors.

• The EBV-associated tumor review focuses on virus-driven malignancies, which may have distinct immune evasion mechanisms compared to non-virally driven solid tumors; generalizability should be interpreted with caution.

• Spatial transcriptomics and scRNA-seq technologies still face challenges including high cost, limited tissue availability, RNA degradation in clinical samples, and the need for specialized bioinformatic pipelines, which may limit broad clinical translation.

• Evidence gaps remain regarding the longitudinal application of scRNA-seq to track immune evasion dynamics from primary diagnosis through relapse in large, prospective solid tumor cohorts.

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## 📋 Summary

**Clinical Summary**:

• Single-cell transcriptomic analysis — particularly scRNA-seq and its integration with spatial transcriptomics and computational transfer learning — represents a transformative approach for dissecting immune evasion mechanisms in solid tumors at unprecedented resolution.

• Key evidence-based takeaway: scRNA-seq enables the identification of exhausted T-cell states, immunosuppressive stromal populations, rare therapy-resistant subclones, and spatially organized immune exclusion zones — all of which are mechanistically linked to tumor relapse and immune evasion.

• Practical recommendation: Integrating multi-omics approaches (genomics, transcriptomics, spatial profiling) with single-cell resolution is increasingly recognized as essential for building a complete molecular taxonomy of the TME, identifying predictive biomarkers of relapse, and designing rational combination therapies targeting immune evasion.

• For translational or clinical research applications of these technologies, collaboration with specialized bioinformatics teams and reference to current institutional and national oncology guidelines is strongly advised, as methodological standards and clinical interpretation frameworks continue to evolve rapidly.

## 🧪 Methodology

### 🔬 Methodology Summary from Top 4 Studies

**Reference # 2:** Huang L, Deng X, Xi Z, Huan X, Mao J, Li X. (2026)

**DOI:** https://doi.org/10.2147/ijgm.s602509

**Study Type:** Review

**Design:** Systematic narrative review of multi-omics biomarkers and spatiotemporal technologies in thyroid cancer precision oncology
**Sample Size:** Not specified
**Duration:** Not specified

**Model/Population:**

- Published literature on thyroid cancer biomarkers, multi-omics technologies, and clinical translation studies; notes specific focus on Asian cohorts for ancestry-specific molecular divergence

**Intervention:**

- Treatment: Not applicable (review)
- Comparator: Not applicable
- Parameters: Not applicable

**Methodology:**

- Systematic delineation of multi-dimensional TC biomarker landscape across genomic, transcriptomic, epigenetic, and proteomic layers
- Coverage of Liquid Biopsy 2.0 including ctDNA-based MRD detection and exosomal multi-omics for non-invasive surveillance
- Evaluation of single-cell sequencing and spatial transcriptomics for intratumoral heterogeneity analysis
- Clinical translation lens: genomic classifiers (e.g., ThyroSeq v3), biomarker-guided therapy de-escalation/intensification, and AI/PDO integration

**Outcomes:**

- Diagnostic accuracy of genomic/epigenetic biomarkers for Bethesda III/IV nodules
- Biomarker utility in RAI-refractory differentiated TC and anaplastic thyroid carcinoma
- Clinical applicability of liquid biopsy for longitudinal surveillance and MRD detection

- Potential of AI models, patient-derived organoids, and metabolic markers for future integration

*Focus: This review synthesizes the evolving multi-omics biomarker landscape and emerging spatiotemporal technologies to establish a precision oncology framework spanning early screening, diagnosis, tailored therapy, and dynamic monitoring in thyroid cancer.*

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**Reference # 3:** Mondal O, Kiruba B, Sudhakaran SL, Sundararajan V. (2025)

**DOI:** https://doi.org/10.3389/fonc.2025.1685565

**Study Type:** Review

**Design:** Comprehensive narrative review integrating multiple technologies for TME analysis in endometrial cancer
**Sample Size:** Not mentioned
**Duration:** Not mentioned

**Model/Population:**

- Published studies on endometrial cancer tumour microenvironment using IHC, scRNA-seq, and spatial transcriptomics

**Intervention:**

- Treatment: Not applicable
- Comparator: Not applicable
- Parameters: Not applicable

**Methodology:**

- First comprehensive review combining scRNA-seq, spatial transcriptomics, and IHC in endometrial cancer
- Integration of conventional (IHC) and emerging (scRNA-seq, ST) technologies for TME characterization
- Focus on tumour heterogeneity deconstruction and cell population identification
- Synthesis of biomarker discovery and therapeutic target identification across methodologies

**Outcomes:**

- Tumour microenvironment composition and dynamics
- Cell population roles in treatment response
- Key biomarkers and therapeutic targets
- Cell-cell interactions within the TME

*Focus: This review synthesizes IHC, scRNA-seq, and spatial transcriptomics findings to provide a comprehensive understanding of the tumour microenvironment in endometrial cancer.*

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**Reference # 4:** Ma X, Zuo Z, Shi W, Sun Y. (2026)

**DOI:** https://doi.org/10.3389/fphar.2026.1786561

**Study Type:** Review

**Design:** Narrative review integrating computational pharmacology with cell biology using a closed-loop 'algorithm prediction-mechanism elucidation-drug intervention' strategy
**Sample Size:** Not mentioned
**Duration:** Not mentioned

**Model/Population:**

- Large-scale cell line datasets, clinical single-cell data, spinal cord injury models (macrophage polarization), osteoporosis models (osteogenic differentiation)

**Intervention:**

- Treatment: Decitabine, benzofuran derivatives, small-molecule drugs targeting disease-associated cell fates
- Comparator: Not mentioned
- Parameters: Not specified; drugs used to reverse macrophage polarization imbalance and osteogenic differentiation disorders

**Methodology:**

- Deep Transfer Learning and Domain Adaptation frameworks (scDEAL, SCAD) to transfer pharmacological knowledge from cell lines to clinical single-cell data
- Virtual prediction of cellular drug sensitivity at single-cell resolution without experimental labels
- Analysis of chemotherapy-induced transcriptional stress states and co-evolutionary mechanisms with inflammatory stromal cells
- Integration of algorithmic drug sensitivity prediction with mechanistic elucidation and small-molecule drug intervention

**Outcomes:**

- Predicted single-cell drug sensitivity
- Reversal of disease-associated cell fates
- Macrophage polarization balance in spinal cord injury

• Osteogenic differentiation restoration in osteoporosis

*Focus: This review proposes an integrated computational-biological paradigm combining single-cell transfer learning algorithms with small-molecule drugs to predict and reverse disease-associated cell fates in heterogeneous disease microenvironments.*

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**Reference # 5:** Carnero A. (2026)

**DOI:** https://doi.org/10.7150/ijbs.130014

**Study Type:** Review

**Design:** Narrative review providing a Darwinian/evolutionary perspective on tumor biology and cancer progression
**Sample Size:** Not mentioned
**Duration:** Not mentioned

**Model/Population:**

• Published literature on tumor evolution, tumorigenesis, tumor microenvironment, and cancer therapies

**Intervention:**

• Treatment: Not applicable (review article)

• Comparator: Not applicable

• Parameters: Not applicable

**Methodology:**

• Applies Darwinian evolutionary theory as a conceptual framework to interpret tumor development and progression

• Covers tumor heterogeneity and plasticity from a biological/evolutionary standpoint

• Integrates topics from tumorigenesis to therapy resistance within an evolutionary model

• Examines tumor-microenvironment interactions and immune system response through an evolutionary lens

**Outcomes:**

• Tumor growth and progression mechanisms

• Metastasis formation and tissue invasion

• Therapy resistance acquisition

- Tumor heterogeneity and plasticity

*Focus: This narrative review frames tumors as biological entities subject to Darwinian evolutionary principles to better understand cancer progression, treatment resistance, and therapeutic strategies.*

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### 📊 Methodological Patterns Across Studies:

**Study Types:**

- Review: 4 studies

**Research Models:**

- Literature: 3 studies

- Multiple: 1 study

**Interventions Studied:**

- Not applicable (review)

- Decitabine, benzofuran derivatives, small-molecule drugs targeting disease-associated cell fates

- Not applicable (review article)

- Not applicable

### 💡 Insights for Research Design:

**From Review/Meta-Analysis:**

- Note inclusion criteria for study selection

- Review analytical approaches for data synthesis

- Consider scope when planning systematic reviews

**General Recommendations:**

- Methodological consistency aids reproducibility

- Most commonly used approaches may have better validation

- Consider variations when adapting protocols to your context

### ⚠️ Important Note:

These summaries are extracted from abstracts, which provide limited methodological detail.

For complete experimental protocols:

- Access full-text articles via DOI links below
- Review Materials & Methods sections thoroughly
- Check supplementary materials for detailed procedures
- Consider contacting authors for specific methodological questions
- Verify protocols match your research context and regulatory requirements

## References


References:

- Epstein-Barr virus-associated tumors: commonalities in pathogenesis and the tumor immune microenvironment.

Authors: Wang X, Hu D, Li R, Liao W, Li C, Liu Q, Li J, Li Q, Guo W, Wang L, Zhang S, Zhao Y
DOI: https://doi.org/10.3389/fimmu.2026.1791347

- Precision Thyroid Oncology: A Review of Multi-Omics Biomarkers and Spatiotemporal Technologies.

Authors: Huang L, Deng X, Xi Z, Huan X, Mao J, Li X
DOI: https://doi.org/10.2147/ijgm.s602509

- Navigating tumour microenvironment in endometrial carcinoma: a comprehensive review integrating immunohistochemistry, single-cell RNA-sequencing and spatial transcriptomics.

Authors: Mondal O, Kiruba B, Sudhakaran SL, Sundararajan V
DOI: https://doi.org/10.3389/fonc.2025.1685565

- Algorithmically defined therapeutic targets: integrating single-cell transfer learning frameworks with small molecule drugs to reverse disease-associated cell fates.

Authors: Ma X, Zuo Z, Shi W, Sun Y
DOI: https://doi.org/10.3389/fphar.2026.1786561

- A Darwinian Perspective on Tumor Evolution.

Authors: Carnero A
DOI: https://doi.org/10.7150/ijbs.130014

- Mitochondrial Hijacking and MicroRNA Crosstalk: Cancer Stem Cell-Mediated Immune Evasion and Metabolic Plasticity in the Tumor Microenvironment.

Authors: Ashrafian Bonab M, Salehi S, Aghababaie A, Amini A, Alizadeh H, Behnam B
DOI: https://doi.org/10.3390/cancers18101611

- Cancer stem cells and post-therapy tumour recurrence: a systematic review of mechanistic pathways and translational gaps.

Authors: Barjij I, Meliani M
DOI: https://doi.org/10.3332/ecancer.2025.2016

- A unified single-cell atlas of HNSCC: Toward characterizing HPV- and sex-associated TME variability.

Authors: Conde-Lopez C, Marripati D, Besso MJ, Roscher M, Han R, Hadiwikarta WW, Elkabets M, Hess J, Kurth I
DOI: https://doi.org/10.1016/j.isci.2026.115863

- Single-cell insights into tumor microenvironment heterogeneity and plasticity: transforming precision therapy in gastrointestinal cancers.

Authors: Weng J, Ju F, Lyu Z, Fan N, Smit DJ, Xu W, Wu X, Becker P, Xu Y, Schweiger MR, Hillmer AM, Harwig R, Gul S, Link A, Meder L, Fang N, Dong Q, Bruns CJ, Ren N, Zhao Y
DOI: https://doi.org/10.1186/s13046-025-03567-5
8 | Top 1%

- RNA sequencing in ovarian cancer research: a comprehensive review.

Authors: Shen F, Li C, Li Y, Shen Y, Han F
DOI: https://doi.org/10.1186/s13048-025-01888-9
2 | Top 5%

- Chemoradiation Reprograms Tumor Cells and the Immune Microenvironment in Cervical Cancer.

Authors: Sandoval TA, Li Y, Muhammad N, Desai T, Jayasinghe RG, Zeeshan S, Jayachandran K, Inkman MJ, Waters MR, Msengi ENS, McKinnish TR, Hatipoglu I, Paschoalini Mafra AC, Anwar M, Hu D, Bhatt DP, Lander VE, Mashl RJ, Houston A, Chen L, Contreras J, Robinson CG, Davies SR, Belmar J, Li S, Major MB, DeNardo DG, Markovina S, Edelson BT, Zhang J, Ding L, Schwarz JK
DOI: https://doi.org/10.1158/0008-5472.can-25-3776
2 | Top 5%

- Terminally exhausted CD8+ T cells in solid tumors: biology, biomarker potential and translational tools for precision oncology.

Authors: Guo X, Ma S, Wang J, Fu Y, Ma W
DOI: https://doi.org/10.3389/fimmu.2025.1709852
8 | Top 1%

- Tumor heterogeneity assessment using single-cell RNA sequencing (scRNA-seq): applications in lung cancer for diagnosis and treatment.

Authors: Bica C, Zanoaga O, Pop L, Ciocan C, Raduly L, Nuțu A, Berindan-Neagoe I, Bender A
DOI: https://doi.org/10.3389/fimmu.2025.1693784
2 | Top 5%

- Spatiotemporal dynamics of radioresistance: decoding macrophage-driven radioprotective niches through temporal-spatial reprogramming.

Authors: Zhang M, Zhang X, Song X, Bai R, Qiao Q, Wei M, Zhao L
DOI: https://doi.org/10.1186/s12943-026-02598-6

• Metabolic collusion driving immune evasion in cholangiocarcinoma: unmasking the dual control of the immuno-metabolic microenvironment.

Authors: Xue J, Zhang L, Zhang K, Wu Y, Zhou K, Lu X

DOI: https://doi.org/10.3389/fimmu.2025.1697056

1 | Top 5%

• The landscape of responses to neoadjuvant immunotherapy in resectable Kirsten rat sarcoma viral oncogene homolog-mutant lung adenocarcinoma: Clinical heterogeneity and correlative immunologic analysis.

Authors: Wu S, Niu J, Chen X, Li J, Tang Q, Yang Z, Gao S

DOI: https://doi.org/10.1002/ctm2.70670

• Rethinking p16, p53, and HPV in HNCSCC through lessons from glioblastoma subclonal evolution toward patient-centric N-of-1 single-cell RNA sequencing paradigm.

Authors: Lee HM, Li SC

DOI: https://doi.org/10.12998/wjcc.v13.i32.104208

• Spatiotemporal dynamics of tumor-associated neutrophils: bridging the gap between cancer progression and immunotherapy.

Authors: Chu X, Ma J, Li S, Wang M, Tian Y, Lv C

DOI: https://doi.org/10.1186/s12943-026-02570-4

2 | Top 5%

• From Spatial Epigenomes to Clinical Diagnostics: Integrative Methylomics Across Scales and Modalities.

Authors: Kinzhebay A, Zhanymbetova A, Yerkos A, Zhetpisbay Z, Imanbek R, Salybekov AA

DOI: https://doi.org/10.3390/ijms27104377

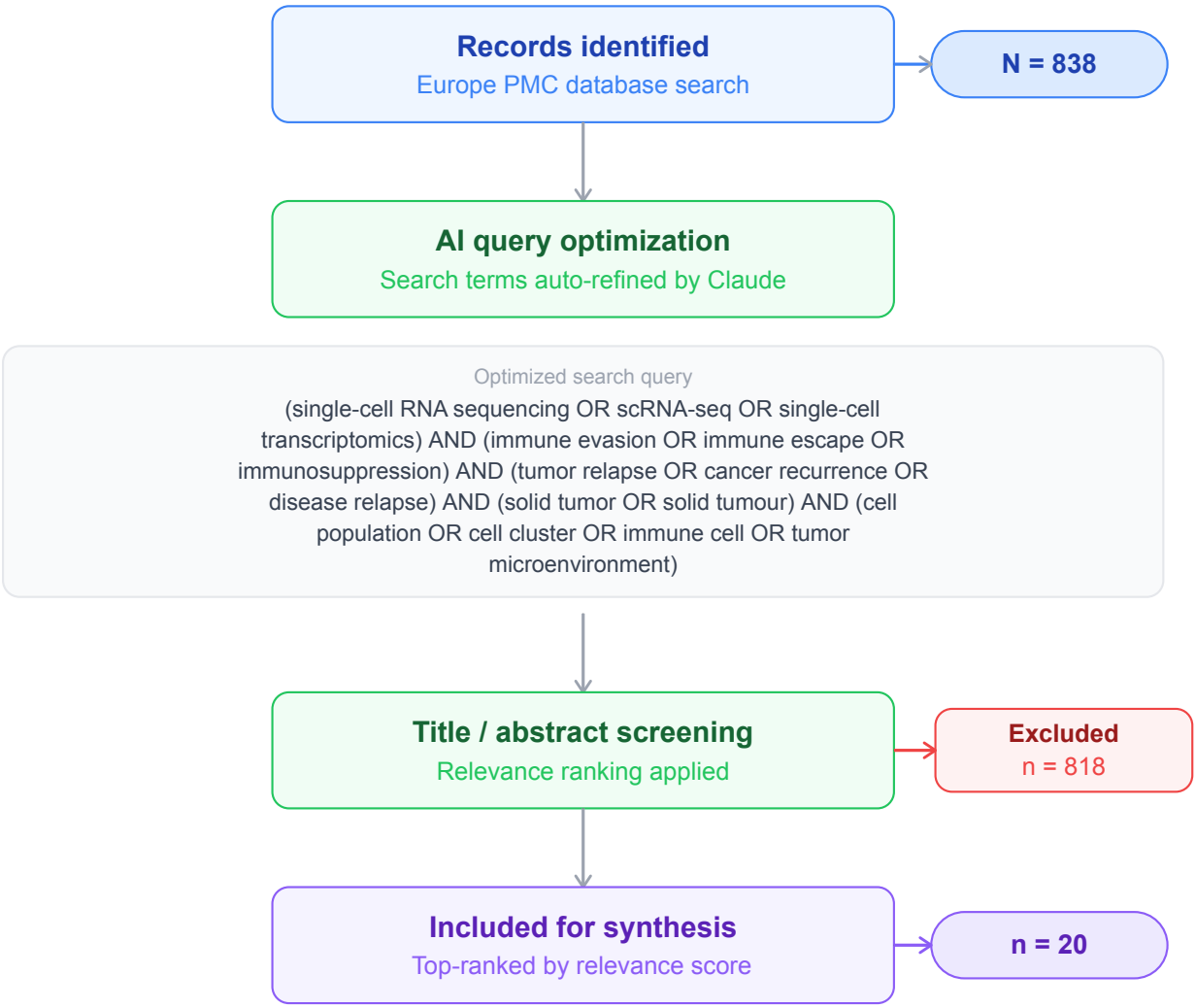
• Clinical Significance of Biomarkers in Oropharyngeal Squamous Cell Carcinoma: Recurrence Prediction and Treatment Response.

Authors: Chen Y, Zhang W, Gao X, Xing K, Ren Y, Hu J, Xie Z, Zhou P

DOI: https://doi.org/10.1002/cnr2.70539

# Screening Results Flow

Europe PMC · AI-assisted relevance screening




**⚠ Abstract-based screening only**

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Full-text screening requires institutional access and must be completed by the user.
The full-text assessment stage of the PRISMA flow chart is not included in this output.