# Article information:

ApoE2, ApoE3 and ApoE4 Differentially Stimulate APP Transcription and Aβ Secretion - PMC
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5310835/>

# Article summary:

1. ApoE isoforms (ApoE2, ApoE3, and ApoE4) have different effects on Alzheimer's disease (AD) pathogenesis, with ApoE4 being the most important genetic risk factor for AD and ApoE2 being protective.

2. ApoE secreted by glia stimulates neuronal Aβ-production with an ApoE4>ApoE3>ApoE2 potency rank order.

3. The molecular mechanism involves ApoE-binding to ApoE-receptors, activating dual-leucine zipper kinase (DLK), a MAP-kinase kinase kinase that then activates MKK7 and ERK1/2 MAP-kinases. Activated ERK1/2 induces cFos phosphorylation, stimulating the transcription factor AP-1, which in turn enhances transcription of amyloid-β precursor protein (APP) and thereby increases amyloid-β levels.

# Article rating:

Appears moderately imbalanced: The article provides some useful information, but is missing several important points or pieces of evidence that would be required to present the discussed topics in a balanced and reliable way. You are encouraged to seek a more balanced perspective on the presented issues by exploring the provided research topics and looking at different information sources.

# Article analysis:

该文章提出了一个新的信号转导途径，即ApoE激活非经典MAP-kinase级联反应，增强APP转录和淀粉样β合成。然而，该文章存在一些偏见和不足之处。

首先，该文章没有考虑到其他可能影响AD发病的因素。例如，环境因素、基因多态性、生活方式等都可能对AD的发病风险产生影响。因此，仅仅将ApoE4作为AD最重要的遗传风险因素是片面的。

其次，该文章没有提供足够的证据来支持其主张。虽然作者通过使用ES细胞衍生的人类神经元表明ApoE由胶质细胞分泌能够刺激神经元Aβ产生，并且具有ApoE4>ApoE3>ApoE2效力顺序，但这并不能证明ApoE是AD发病机制中的关键因素。

此外，在描述信号转导途径时，作者没有探索其他可能存在的途径或反驳其他可能解释结果的假设。例如，在描述DLK激活ERK1/2 MAP-kinases时，作者没有考虑到其他可能介导这个过程的蛋白质或信号通路。

最后，在讨论结果时，作者没有平等地呈现双方观点。他们只提到了ApoE4作为AD遗传风险因素，并未探讨其他观点或假设。

总之，尽管该文章提出了一个新颖且有趣的假说，但它存在一些偏见和不足之处。未来需要更多实验数据和更全面、客观地考虑各种可能性才能更好地理解AD发病机制。

# Topics for further research:

* Other factors affecting AD risk
* Insufficient evidence to support the claim
* Other possible signaling pathways or hypotheses
* Lack of equal presentation of opposing views
* Need for more experimental data
* Comprehensive and objective consideration of possibilities

# Report location:

<https://www.fullpicture.app/item/e149755c87008318ce286745f6217f44>