Curcumin Promotes Hematoma Resolution Following Intracerebral Hemorrhage via a CD36-dependent Mechanism

James Campbell, Cargill Alleyne Jr. M.D., Krishnan Dhandapani Ph. D.
Department of Neurosurgery, Georgia Regents University
1120 Fifteenth St, Augusta, GA 30901
Intracerebral Hemorrhage (ICH)

• 15% of strokes – about 120,000 each year
• Caused by hypertension or amyloid angiopathy
• 40% mortality rate in the first month
• Least treatable form of stroke
Intracerebral Hemorrhage (ICH)

- Hematoma volume is an independent predictor of mortality and long-term deficits
- However, surgical intervention remains limited
- Need for alternative therapeutics
Curcumin

- *Curcuma longa*
- Potent anti-inflammatory agent
- Reduces vascular inflammation and acute injury after traumatic brain injury and subarachnoid hemorrhage
- Available through oral administration at >12g/day
Experimental ICH Model

• Stereotaxic injection bacterial type IV collagenase into striatum
Curcumin significantly reduces BBB permeability after ICH 24 HOURS POST-ICH

**EVANS BLUE PERMEABILITY**

(µl plasma x g brain wt⁻¹ x hr⁻¹)

<table>
<thead>
<tr>
<th></th>
<th>SHAM</th>
<th>ICH</th>
<th>CCM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>24h</strong></td>
<td>***</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Curcumin significantly reduces cerebral edema after ICH

**24 HOURS POST-ICH**

**72 HOURS POST-ICH**
Curcumin significantly improves neurological outcomes after ICH

![Graph showing neurological scale scores over time for SHAM, ICH, and ICH + CCM groups.](image)
Curcumin induces hematoma resolution at 72 hours
Curcumin significantly reduces hemoglobin content when administered up to 3 hours post-ICH.
CD36

- Class B scavenger receptor
- Mediates lipid metabolism, inflammation, host defense, phagocytosis
- Promotes phagocytosis in monocyte lines
- Has been implicated in spontaneous hemATOMA resolution
Curcumin increases CD36 in the peri-hematoma area after ICH
Curcumin promotes CD36 expression and phagocytosis in murine microglia
Conclusions

• Curcumin reduces hematoma volume, secondary injury, and improves outcomes following ICH
• Curcumin increases phagocytosis via CD36 in murine microglia
• Curcumin increased expression of CD36 in perihematoma area after ICH
• Curcumin may provide a novel therapeutic strategy for hematoma resolution after ICH
Acknowledgments

- Dr. Krishnan Dhandapani, Ph. D
- Dr. Cargill Alleyne, Jr., M.D.
- Dhandapani Lab
  Sangeetha Sukamari-Ramesh, Ph.D
  Melanie King, Ph.D
  Jay McCracken, M.D.

- Dr. Steffen Meiler, M.D.
- Marlene Wade, B.S.

NIH: NS075774; NS065172
AHA: BGIA2300135