#ISC26

Yale

ANTI-INFLAMMATORY MECHANISMS OF ANTI-SDC2 MAB VB-001 CONTRIBUTING TO NEUROPROTECTION AFTER ISCHEMIC STROKE

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American Stroke Association.
A division of the American Heart Association.

Anti-Inflammatory Mechanisms of Anti-Sdc2 Mab VB-001 Contributing to Neuroprotection After Ischemic Stroke

Federico Corti, PhD

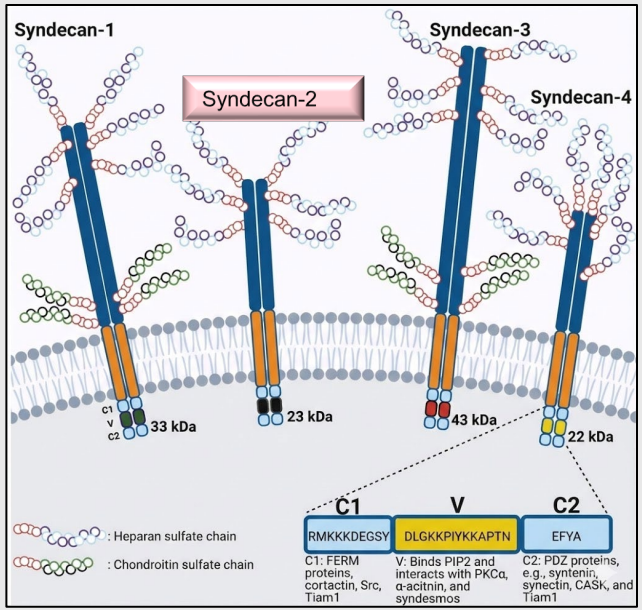
FINANCIAL DISCLOSURE:

Grant/Research Support: VST Bio, Corp., 4653 Carmel Mountain Road, St 308, PMB 1015, San Diego, CA 92130, USA

Federico Corti, PhD and Michael Simons, MD

Cofounders of VST Bio Corporation

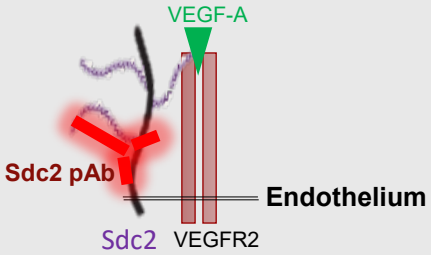
Sdc2 is a membrane proteoglycan that regulates vascular leak and activation of inflammatory monocytes

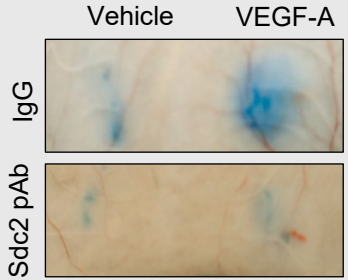


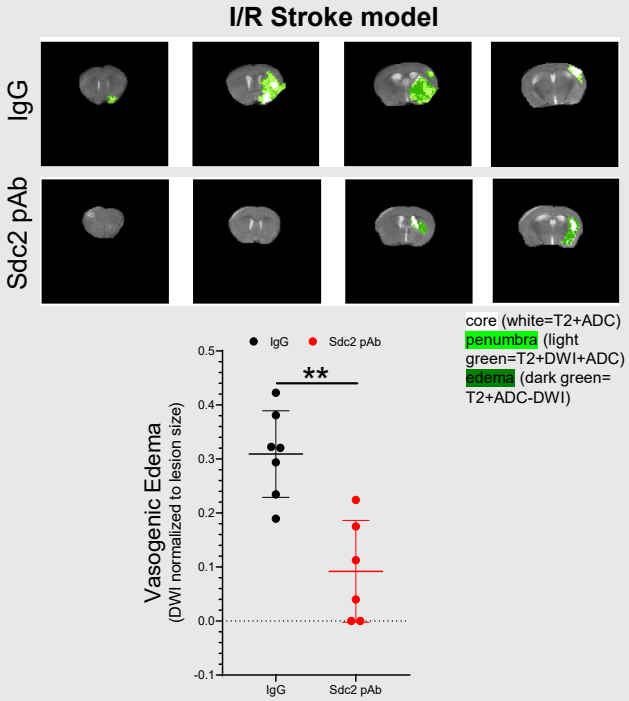
Aniko Keller-Pinter. Cancers (Basel) (2021). PMID: 34282767

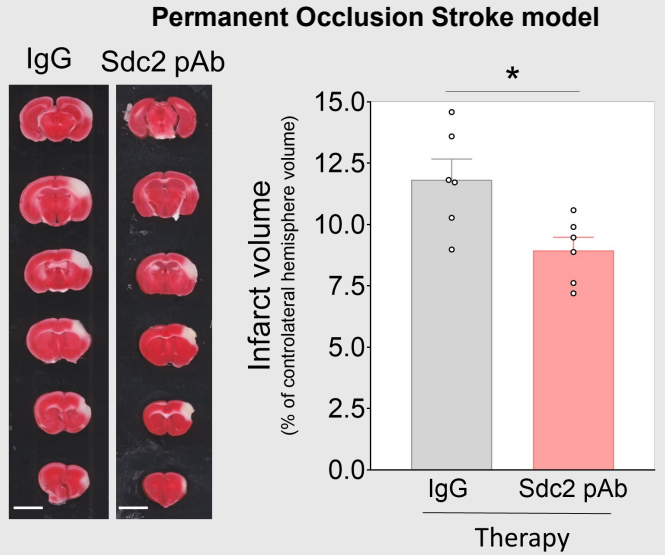
- Sdc2 is expressed in endothelial cells, classical CD14^{+} monocytes, neutrophils, fibroblast and SMC.
- Endothelial cells: Sdc2 is a specific coreceptor for VEGFR2 and tightly controls VEGF-induced vascular leak and inflammatory edema
- Monocytes: Sdc2 forms a molecular complex with immune-checkpoint VISTA that modulates activation state/response to inflammatory stimuli
- Sdc2 genetic deletion in mice: we observe improved outcome in diseases model where vascular leak and/or infiltration of highly inflammatory monocytes play a detrimental role. These include:
  - stroke (neuroprotection)
  - sepsis (decreased mortality)
  - AMI (reduced progression to HF)
  - wet AMD (reduced retinal edema/displacement)
  - atherosclerosis (reduced plaque burden)

Anti-syndecan-2 polyclonal antibody (Sdc2 pAb) blocks vasogenic edema and promotes neuroprotection



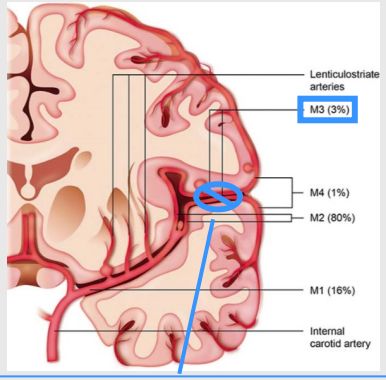






Corti et al. Nature Communications (2019). PMID: 31064993
Corti et al. Nature Cardiovascular Research (2022). PMID: 36212522
Corti et al. Translational Vision (2025). PMID: 36212522

Humanized monoclonal anti-human Sdc2 (Sdc2 mAb) confers neuroprotection in a NHP ischemic stroke model



Occlusion of the M3 branch
(3 hours ischemia)

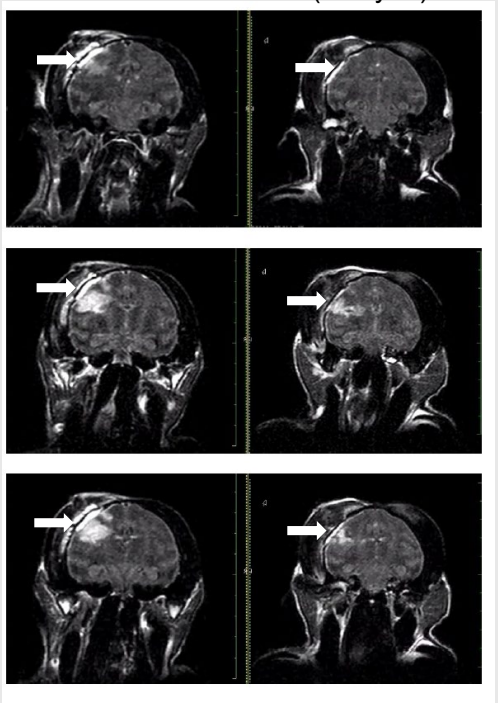
Reperfusion and I.V injection:
Group 1. Vehicle

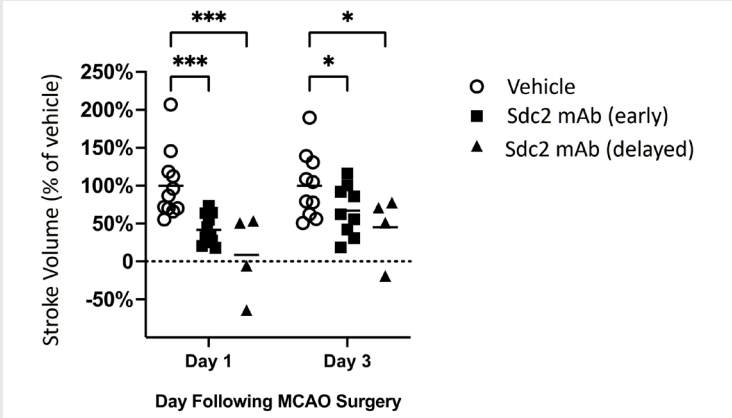
Group 2. Sdc2 mAb (early)
- 3 hours post occlusion -

Group 3. Sdc2 mAb (delayed)
- 6 hours post occlusion -

Day 3 (2d-FLAIR)

Vehicle | anti-Sdc2 mAb (delayed)





Syndecan-2 expression is associated to proinflammatory activities of the CD14^{+}CD16^{+} monocyte subset

Front Immunol. 2025 Feb 20:16:1475480. doi: 10.3389/fimmu.2025.1475480. eCollection 2025.

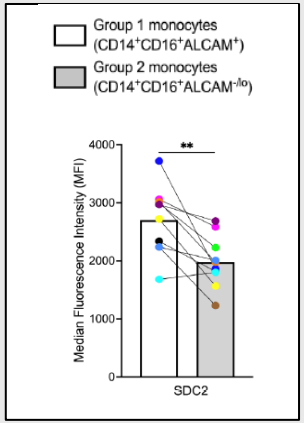
Single-cell analysis of CD14^{+}CD16^{+} monocytes identifies a subpopulation with an enhanced migratory and inflammatory phenotype

Vanessa Y Ruiz [1], Tina M Calderon [1], Rosiris Leon-Rivera [1], Vanessa Chilunda [1], Jinghang Zhang [2], Joan W Berman [1 2]

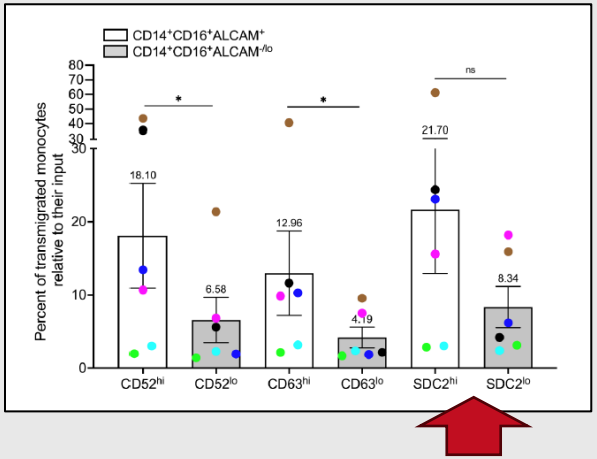
Ruiz et al. *Frontiers in Immunology* (2025). PMID: 40051633

Key Findings:

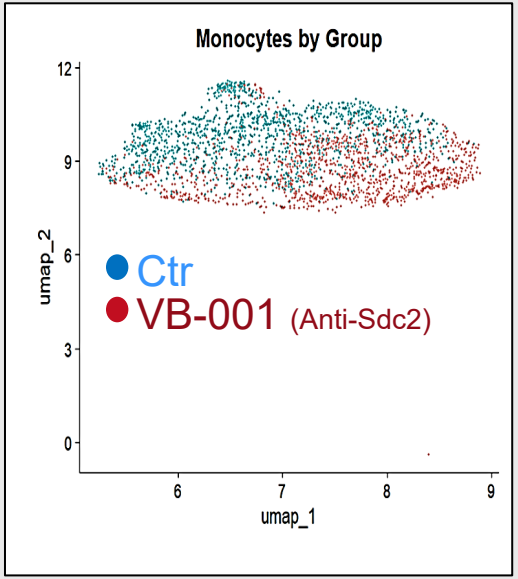
- Sdc2 expression is enriched in a highly proinflammatory monocyte subset (CD14^{+}CD16^{+}ALCAM^{+})

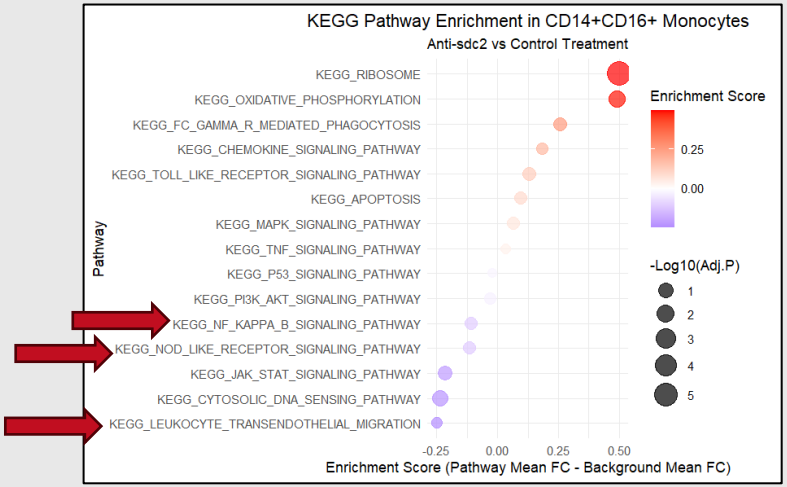


- Sdc2 expression level is positively associated with higher ability of monocytes to transmigrate across a BBB model in vitro (in response to CCL2)

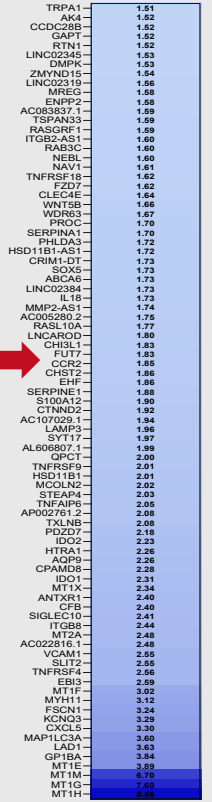


Treatment with VB-001 promotes an anti-inflammatory switch of the CD14^{+}CD16^{+} monocyte subset

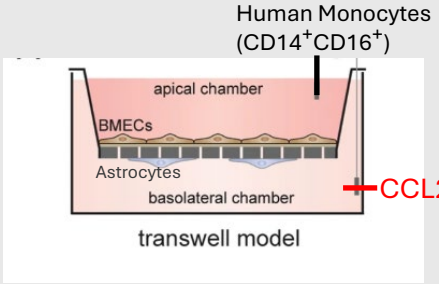


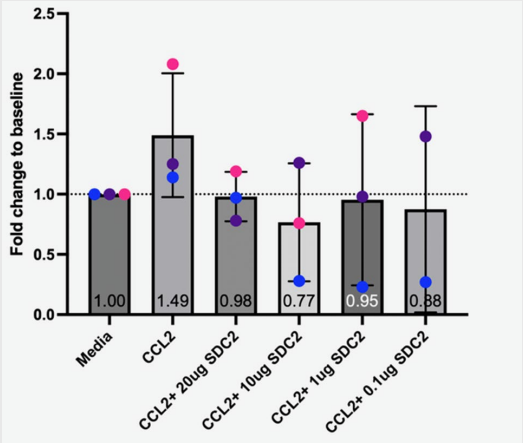


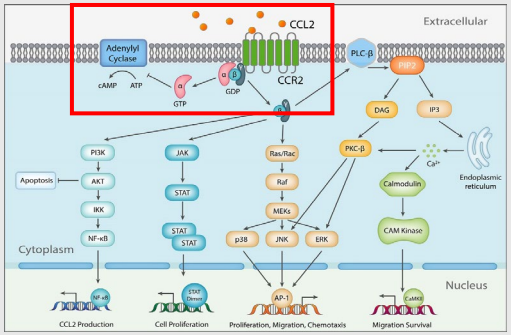
CCR2

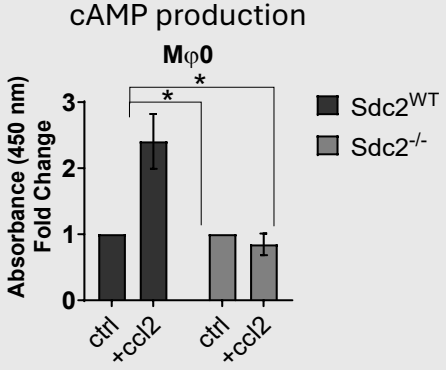


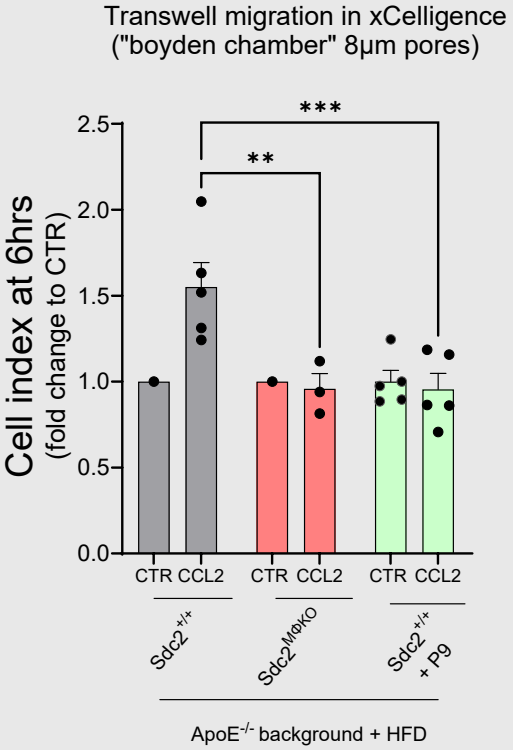
Transmigration across a human BBB model in response to CCL2 is blocked by VB-001 via CCR2 inhibition











Reduced stroke size after Sdc2-specific deletion in monocytes ($Sdc2^{M\varphi KO}$) or with anti-mouse Sdc2 mAb (P9) treatment

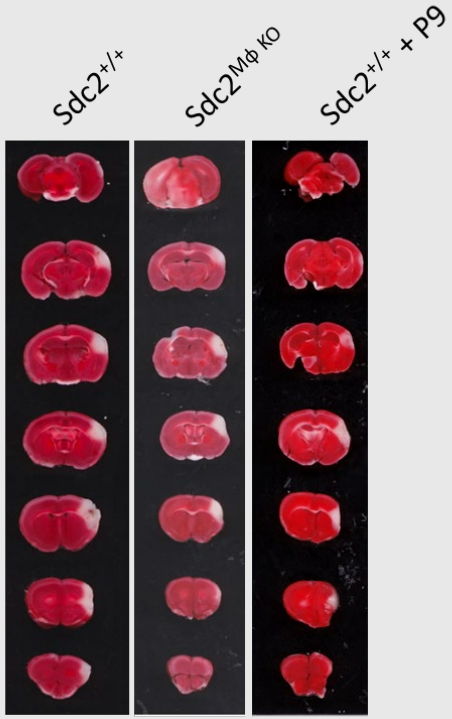
ApoE -/-
background mice

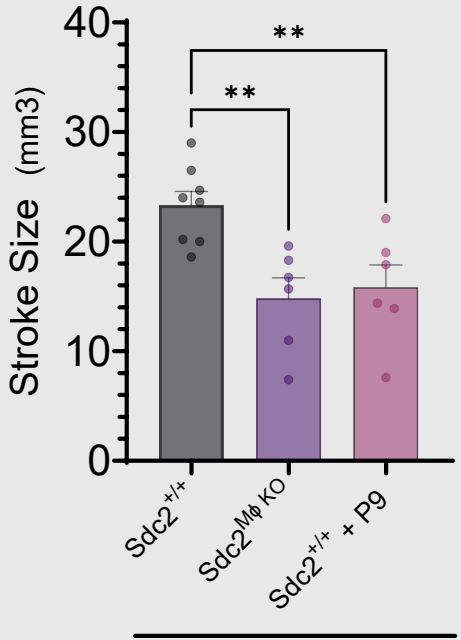
16 weeks High-Fat Diet
(promote hyperlipemia and high count of ly6c circulating monocyte)

Ischemic Stroke
(distal MCA Permanent occlusion)

Antibody treatment
(1 hr after occlusion)

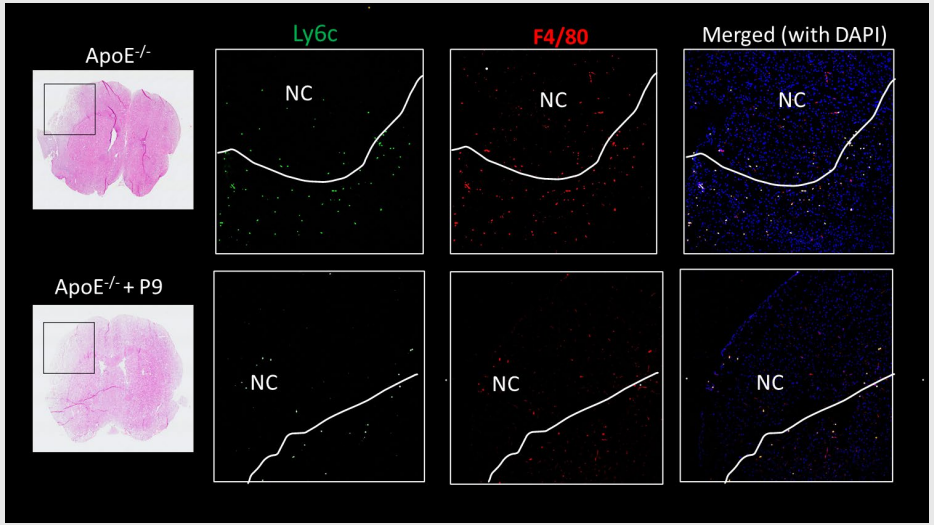
TTC Staining at 24 hours post stroke

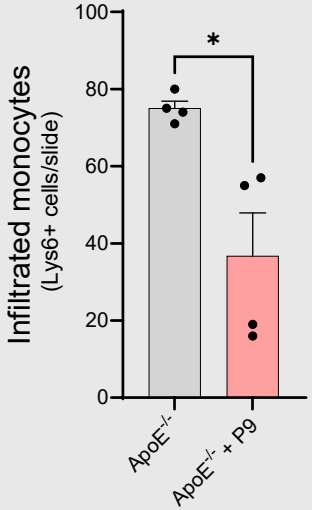


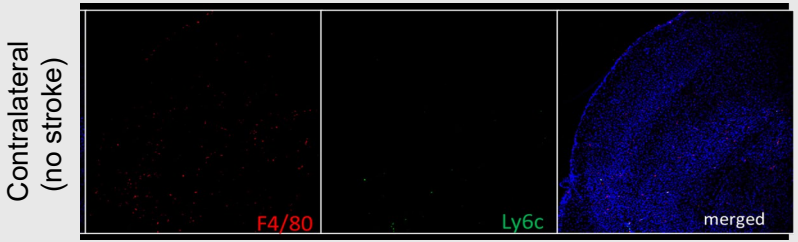


All mice ApoE-/- background
+ 4 months HFD

Treatment with anti-mouse Sdc2 mAb (P9) reduces Ly6C inflammatory monocyte influx into penumbra region post-ischemic stroke

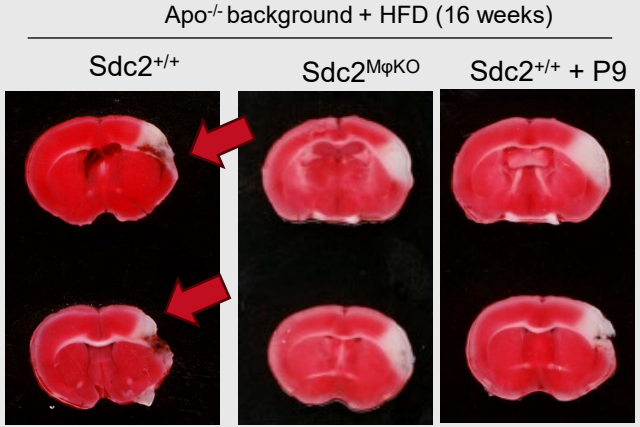


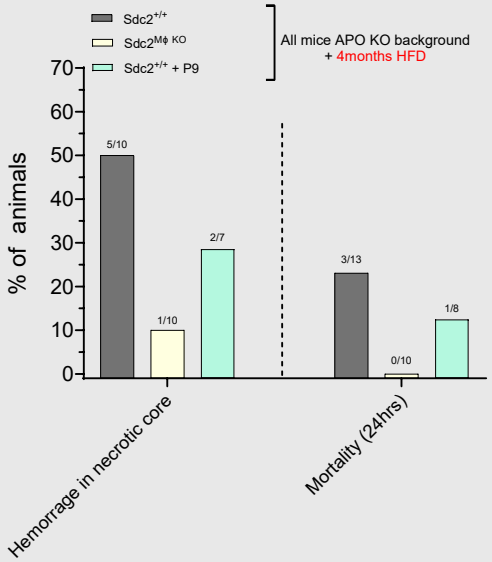


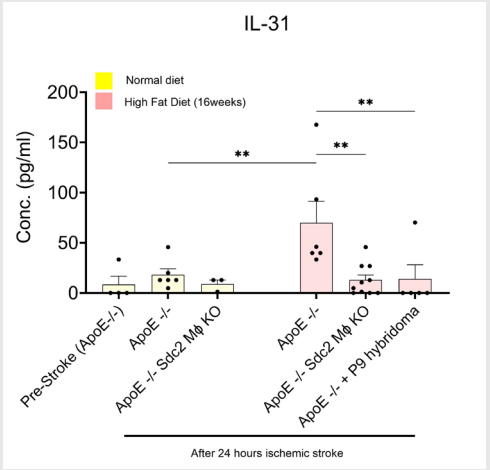


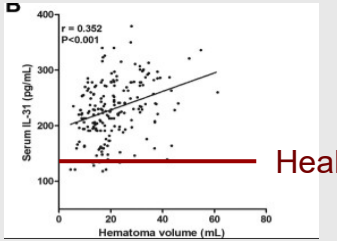
Treatment with anti-mouse Sdc2 strongly reduces frequency of hemorrhagic transformation

- Hemorrhagic transformation (HT) is a serious complication (frequently lethal) occurring in 10 to 40% of ischemic strokes.
- Typically occurs within the **first week, with a median timeframe of 6 days (range 1–27 days)**.
- In patients treated with reperfusion therapy HT usually develops within 24 hours of treatment.









Healthy

Jingfeng Liu et al.
Medicine (Baltimore) 2023 –
PMID: 38306544

VB-001 offers a multi-pronged approach maximizing neuroprotection as well as prevention of hemorrhagic transformation

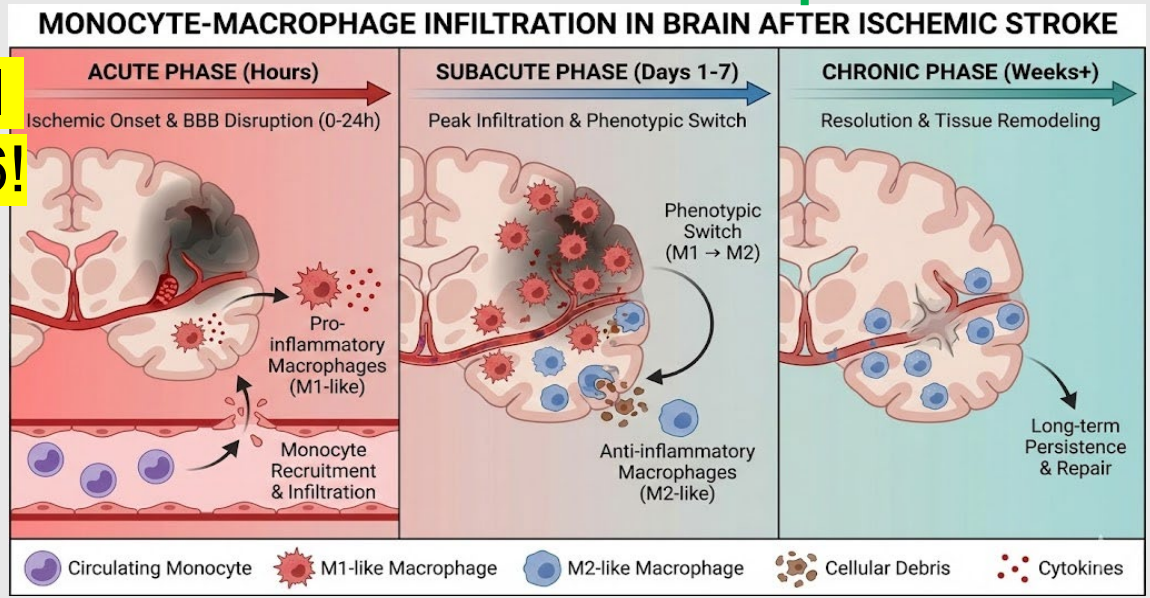
VB-001

- Prevents Hemorrhagic Transformation (HT)
- Blocks infiltration of highly inflammatory monocytes
- Blocks vasogenic edema

Reduced mortality and HT complications

Max Neuroprotection

Phase I clinical trial in Fall 2026!



VB-001, INNOVATION AND EFFECTIVENESS IN ISCHEMIC STROKE

1. VB-001 offers a multi-pronged approach that maximizes neuroprotection by targeting BBB endothelium and inflammatory monocytes

2. VB-001 can reduce the frequency of hemorrhagic transformation (HT) thus reducing serious complications and mortality

3. A long therapeutic window for neuroprotection (up to 24hrs or more) and likely longer for the anti-HT effect

4. No adverse side-effects were observed in extensive use in both mouse and non-human primate model

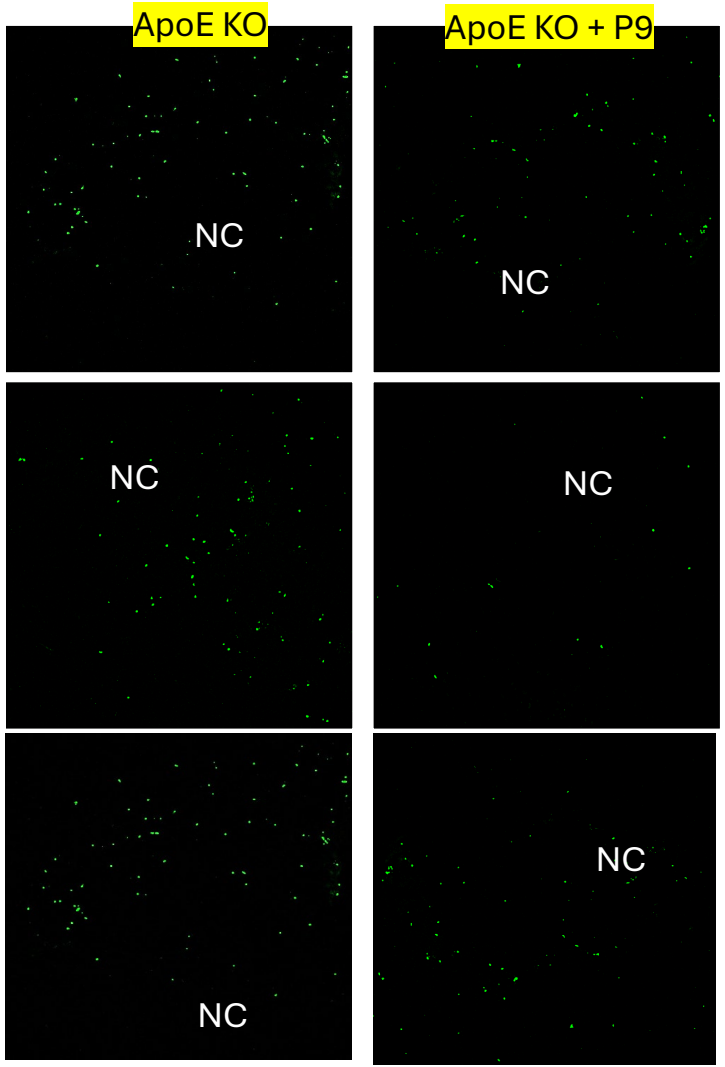
5. Sdc2 mAb may combined with other treatments (e.g. TPA) without interfering with their mechanism of action

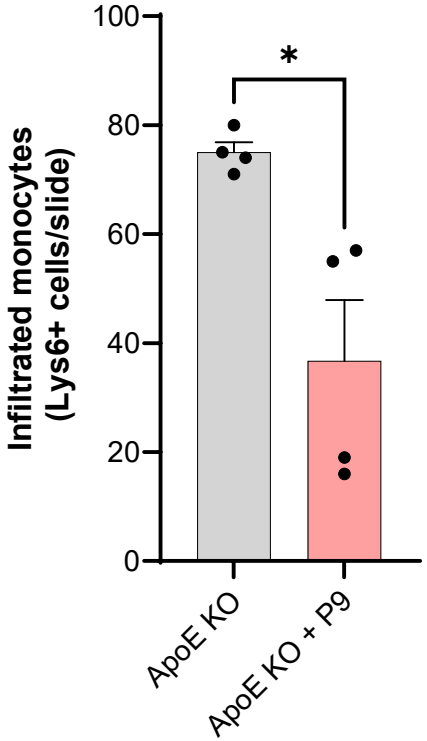
THANK YOU

American Stroke Association.
A division of the
American Heart Association.

#ISC26

International Stroke Conference


ApoE KO
ApoE KO + P9
NC
NC
NC
NC
NC
NC


Infiltrated monocytes
(Lys6+ cells/slide)
100
80
60
40
20
0
*
ApoE KO
ApoE KO + P9