**INTRODUCTION**

- Over 1 million suicide deaths annually: No biomarkers for suicide ideation, attempt, risk, or completion exist (National Institute of Mental Health #1 priority is biomarker identification).
- Lack of effective psychopharmacological medications identification due to the lack of novel molecular targets.
- Blood-Brain Barrier (BBB) Breakdown: Claudin-5 degradation.
- Allows for perivascular intrusion of albumin and immunoglobulin-γ (IgG), the most predominant protein and antibody in the blood, into the brain parenchyma (Fig. 1).
- Claudin-5. Candidate biomarker in other neurological disorders but role in suicide neuropathology remains unelucidated.

**RESULTS/DISCUSSIONS**

**Increased Claudin-5 in Suicide Decedents**
- ELISA identified increased claudin-5 levels in dIPEC of suicide decedents (1.33 mg) than in controls (1.01 mg). 

**CLDN5 is Downregulated in Suicide Decedents**
- Maintenance of the BBB gene ontology in suicide decedents (p=0.05; Table 1).

**CLDN5 CpG Sites Targets**
- Two differentially methylated CpG sites of CLDN5 in chromosome 22 (Fig. 8).
  - cg06315607 (Table 1).
  - cg02486669 (Table 1).

**Neuroinflammation and Claudin-5 Breakdown Association**
- In suicide decedents, increased recent-life stress was associated with greater claudin-5 residue in the dIPEC (p=0.05).
- Claudin-5: Promising objective index that can bridge the gap between behavioral assessments and neuroanatomical anomalies.

**Increased Peripheral Proteins in Suicide Decedents**
- Elevated IL-6 and IL-8 in suicide (p=0.05).
- IL-6- and IL-8 induce transcriptional downregulation of claudin-5.
- BBB compromise: Influx of large peripheral proteins.
- Increased albumin (70 KDa).
- 33% increase (175 KDa) but not significant (p=0.06).
- BBB breakdown in suicide: Greater risk for neurotoxic molecules into the brain increasing vulnerability to altered neurocognition.

**Molecular Docking**
- Escitalopram and Benzodiazepine: Present drugs to treat suicide ideation have low affinity with claudin-5.
- Escitalopram (Fig. 11A) and Benzodiazepine (Fig. 11B) not effective in treating suicide: not effective in targeting claudin-5 levels.
- Doxycycline (Fig. 11A) and alternative medications: restore claudin-5 BBB integrity.

**CONCLUSIONS/FUTURE RESEARCH/APPLICATIONS**

1. First human postmortem study to assess BBB disruption through increased claudin-5 and albumin in the dIPEC of suicide decedents and genomic alterations of CLDN5.
2. Future in vitro assessments should evaluate novel therapeutics promoting claudin-5 for suicide prevention and genetic manipulation of CLDN5 to restore BBB integrity.
3. Claudin-5 and albumin can serve as novel biomarkers to discern high-risk individuals with the severity of suicide risk allowing for earlier interventions.

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