Are We Ready to Translate T-Cell Transmigration in Stroke?

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Stroke research is plagued by failed bench to bedside translation—hundreds of agents that protected rodent brains were not effective when tested in clinical trials. Low reproducibility and predictiveness seem to be hallmarks of preclinical studies in many fields of medicine. It is becoming increasingly clear that, at least partially, low internal and external validity (lack of randomization and blinding, young animals lacking comorbidities), lack of power (small sample sizes), and negative publication bias are to be blamed, because they lead to inflated effect sizes or false-positive results. In the context of the many failures of neuroprotection trials in stroke, it is surprising on how little evidence the ongoing natalizumab stroke trial is based. The negative results of the study by Langhauser et al add further doubt concerning the robustness of this treatment strategy.

It is clear that individual laboratories do not have the resources or incentives to replicate their own or other’s data and to preclinically test novel treatments with the required sample sizes and portfolio of models. This can only be done by international consortia of researchers, acting in a concerted fashion. Some methodological aspects of such preclinical phase III studies can be borrowed from clinical trials; others still need to be developed (eg, European Union–funded Multicenter Preclinical Animal Research Team; http://www.multi-part.org). It is interesting to note that an international consortium coordinated by Arthur Liesz (Munich, Germany) is currently conducting such a preclinical phase III trial for the CD49d antibody, involving laboratories from Germany, France, Italy, and Spain. Results of this trial will be available soon and hopefully help to resolve the issue whether T-cell transmigration is ready for translation. We sincerely hope that natalizumab will not join the list of drugs for which experimental studies delivered ex post evidence why the clinical trial had failed (eg, the German erythropoietin [EPO] trial, the Abciximab Emergent Stroke Treatment [ABESST] II trial, the eliminomab trial).

Disclosures

None.

References


Editorial

See related article, p 1799.

Changes in the adaptive immune system after focal cerebral ischemia are increasingly recognized to critically influence the outcome after stroke. In particular, T lymphocytes have been implicated as mediators of inflammatory brain tissue damage, but also as modulators of tissue remodeling. In addition, reductions in T-lymphocyte cellularity and function are prominent features of stroke-induced immunodepression and may increase the susceptibility to infection after stroke. Are prominent features of stroke-induced immunodepression addition, reductions in T-lymphocyte cellularity and function have been implicated as mediators of inflammatory brain tissue...


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