Meeting report

Arresting mental decline

Molecular Mechanisms of Neurodegeneration, a joint meeting with Neuroscience Ireland, held at University College Dublin, 15–16 March 2005

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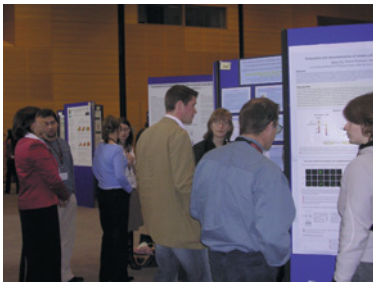
With 98 poster and 30 oral presentations by scientists from 15 different countries, Molecular Mechanisms of Neurodegeneration was one of the largest conferences on this topic ever to take place in Ireland.

The purpose of the meeting was to showcase recent advances in neurodegenerative research, and to highlight the need for the expansion of research in this area. Undoubtedly, both of these objectives were realized. In particular, it was a delight that leading scientists working on Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis shared their recent unpublished data. Three excellent examples of this were presentations by Karen Ashe (University of Minnesotta), Menelas Pangalos (Wyeth Pharmaceuticals) and Dennis Selkoe (Harvard Medical School).



All three reviewed progress on obtaining a better understanding of established therapeutic targets, but Professor Pangalos also shared exciting data about a new drug target. Thanks to work by groups led by Steve Estus[1] and Sidney Strickland[2] it has been accepted that the protein believed to cause Alzheimer's disease, the amyloid β peptide (Aβ), is a plasmin substrate and that the tissue plasmin activator (tPA)/plasminogen system is required for Aβ clearance *in vivo*. However, it has also been demonstrated that activation of plasminogen is antagonized by plasminogen activator inhibitor-1 (PAI-1). Like tPA and plasmin, PAI-1 is a serine protease, and Wyeth have developed small-molecule inhibitors that specifically target PAI-1. In APP (Aβ precursor protein) transgenic mouse models, inhibitors of PAI-1 increased brain levels of plasmin, decreased Aβ burden and recovered cognitive deficits. Plasmin is also involved in fibrinolysis, but no bleeding defects were observed in animals treated with PAI-1 inhibitors.

These results together with data from other presentations raise the very real prospect that rational therapeutic intervention is much closer than many of us could have dared hope just a few short years ago. In this regard, it is my sincere hope that our conference has helped promote the dissemination of knowledge and collaboration necessary to realize progress towards the treatment of diseases once believed to be intractable. And in that spirit, I'd like to thank all those who helped make our meeting a success. I am indebted to all the speakers for their wonderful presentations. Similarly, I am also grateful to Christine Cook from the Biochemical Society's Meetings Office and the other members of the organizing committee for their contributions. Of course, this meeting would not have been possible without the financial support of our sponsors and I thank them for their generosity.

References

1. Tucker, H.M., Kihiko, M., Caldwell, J.N. et al. (2000) J. Neurosci. **20**, 3937–3946
2. Melchor, J.P., Pawlak, R. and Strickland, S. (2003) J. Neurosci. **23**, 8867–8871