

主 論 文 要 旨

報告番号	① 乙 第	号	氏 名	魯 方 琳
主 論 文 題 名 Pharmacological Ischemic Conditioning with Roxadustat Does Not Affect Pain-Like Behaviors but Mitigates Sudomotor Impairment in a Murine Model of Deep Hind Paw Incision (Roxadustatによる薬理的虚血コンディショニングはマウス足掌切開モデルでの疼痛様行動に影響しないが発汗障害を緩和する)				
(内 容 の 要 旨) The involvement of hypoxic response mechanisms in local functional impairments in surgical wounds is unclear. In the present study, tissue hypoxia was characterized in surgical wounds and the role of pharmacological ischemic conditioning (PIC) using roxadustat, an oral prolyl hydroxylase domain enzyme inhibitor, in postoperative local functional impairments was investigated in a murine model of deep hind paw incision. Prominent tissue hypoxia was detected within axons in the nerve bundles underneath surgical wounds. Six-week perioperative PIC using roxadustat failed to ease spontaneous pain-like behaviors; however, it mitigated local sudomotor impairment postoperatively. Upregulation of sympathetic innervation to the eccrine glands was observed in the PIC treated skins collected on postoperative day 21, in accordance with the <i>in vitro</i> study wherein roxadustat promoted neurite growth of sympathetically differentiated PC12 cells. This study suggests that tissue hypoxia is involved in the pathogenesis of local sudomotor dysfunction associated with surgical trauma. Targeting the hypoxic response mechanisms with PIC may be of therapeutic potential in postsurgical local sympathetic impairments that can be present in complex regional pain syndrome.				