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This Week's Citation Classic

Bradley T R & Metcalf D. The growth of mouse bone marrow cells *in vitro.*
Aust. J. Exp. Biol. Med. Sci. **44**:287-300, 1966.
[Dept. Physiol., Univ. Melbourne; and Cancer Res. Unit, Walter and Eliza Hall Inst., Parkville, Victoria, Australia[1]

The article describes the quantitative clonal growth of mouse bone marrow cells *in vitro* using an agar culture system. Neonatal mouse kidney or whole embryo cells were used as feeder cells to stimulate colony development. The colonies were shown to be composed of large mononuclear cells probably phagocytosing agar and cells typical of the early stages of development of mouse granulocytes. [The *SCI*® indicates that this paper has been cited over 545 times since 1966.]

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"The work referred to was initiated by an observation made whilst attempting to start another investigation. **I** had **returned to the** Physiology Department. Melbourne University, from the National Cancer Institute where Lloyd **Law had** made me enthusiastic about thymus studies and Bob Roosa had taught me **the** elements of cell culture, particularly the importance of cloning techniques.

"I wanted to see whether one could detect clonogenic tumour cells in the thymus of AKR mice prior to the obvious tumour development. Don Metcalf and I were collaborating on another project involving thymus and spleen transplants and Don's AKR mouse colony was available, so I started trying to clone thymus, lymph node, and bone marrow cells, the latter two tissues as 'controls' for the thymus Two significant points in the technique were the use of agar to immobilize any progeny developed, which other workers had been starting to use, and the use of feeder cells which had also been recognized as often of use in cloning techniques.

"In the first experiments, the thymus cells failed miserably but small colonies developed from the marrow cells, the growth of which was greatly improved by a variety of feeder cells, particularly neonatal kidney and whole embryo cells. The morphology of the colony cells was an important issue. Don's experience in morphological studies was enlisted as we started trying to identify the cell types in the colonies, an exercise which is still necessary whenever new sources of proliferative factors are used in the system.

"The reason that the paper has been frequently cited is probably because it offered a simple technique for quantitation of both the progenitor cells in normal and pathological conditions and the proliferative factors elaborated by feeder cells or present in body fluids. As such it offered the possibility of resolving some of the problems concerning the control of granulopoiesis and, as emerged more clearly a little later, monocytopoiesis.

"In retrospect, two aspects of the work at this stage always seem important to me. The first point is that it was soon shown that identical colony formation could be obtained using mouse serum to replace the feeder cells which gave the system a more physiological basis. The second point has been that, had we started with any other species, it may well have not succeeded so easily. Perhaps this is a salutary lesson to those who want us to dispense with experimental animal model systems."